INVESTIGATIONS ON THE SYNTHESIS OF NEW PHOTOCHROMIC OXAZINE DERIVATIVES

by

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Thesis presented for the Degree of Doctor of Philosophy

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CONTENTS

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Final thanks are found in Psalm 145.

POSTGRADUATE LECTURE COURSES ATTENDED

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'Topics in Medicinal Chemistry'; Dr G. Stevenson, Dr L. Castro and Dr H. Broughton, Merck, Sharp and Dohme Ltd.: 1997.

'Synthesis of Fine Chemicals'; Prof A. McKillop, University of East Anglia: 1996.

'Protecting and Commercialising Inventions'; Dr R. Pugsley and Dr S. Stephen, Zeneca; Dr J. Brennan, European Patent Office and Dr K. Winton, University of Edinburgh: 1997.

'Current Awareness in Organic Chemistry'; Dr H. McNab, Dr A. Hulme, Dr N. Turner, Dr I. Gosney and Dr R. Paton, University of Edinburgh: 1997.

'Current Awareness in Organic Chemistry'; Dr G. Tennant, Dr J. Sharp, Dr S. Flitsch and Prof R. Ramage, University of Edinburgh: 1998.

'Safety Lectures'; Mr J. Spittle, Merck Ltd.: 1998.

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ABSTRACT

This thesis is concerned with the investigation of new synthetic routes to novel oxazine derivatives which are of potential photochromic importance.

Initial studies were based on previous work at Edinburgh in which the reaction of the lithium salt of 1,2-naphthalenedione 1-oxime with 2-bromo-2,2-diphenylacetaldehyde was found to afford an oxime ether which was reduced with triphenylphosphine to afford 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine. Similarly, 2,2-diphenyl-2*H*-naphth[1,2-*b*]-1,4-oxazine was prepared in a parallel synthetic strategy using 1,2-naphthalenedione 2-oxime as key starting material. To facilitate the expansion of this strategy, further bromo-aldehydes functionalised with variously substituted aromatic moieties were prepared. Reaction of these bromo-aldehydes with 1,2-naphthalenedione 1-oxime lithium salt, followed by reduction of the resulting oxime ethers, facilitated the synthesis of a number novel 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazine derivatives.

On encountering problems in the synthesis of certain diaryl bromo-aldehydes, the synthesis of alternative diarylacetaldehyde derivatives amenable to reaction with naphthalenedione oxime lithium salts was attempted. Several 2,2-diaryl-2-hydroxyacetaldehydes were prepared and their conversion to previously inaccessible halogeno-aldehydes was investigated.

Using 1,2-naphthalenedione 2-oxime and 9,10-phenanthrenedione 9-oxime as starting materials, the aforementioned methodologies were applied to the respective syntheses of 2,2-diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazines and 2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines. Investigations were also made into the mechanism of the formation of these novel photochromic species. The chemistry of certain novel naphth-1,4-oxazines and phenanthro-1,4-oxazines was investigated and they were found to behave as cyclic imines.

Photochromic 3,3-diaryl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazines were also prepared. However, the attempted synthesis of 2,2-diphenyl-2*H*-acenaphtho[1,2-*b*]-1,4-oxazine was unsuccessful.

Work was also undertaken on various synthetic routes to diarylnaphth-1,3-oxazine derivatives. Initial attempts were based on the preparation and cyclisation of 1-benzoylaminomethyl-2-naphthol. This having failed, an alternative approach involving the reaction of diarylketimines with 2-hydroxy-1-naphthaldehyde was investigated and successfully afforded 3,3-diaryl-3*H*-naphth[1,2-*e*]-1,3-oxazines.

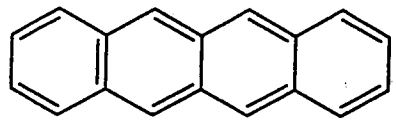
In parallel with these studies the analogous syntheses of 2,2-diphenyl-2*H*-naphth[2,1-*e*]-1,3-oxazine and 2,2-diaryl-2*H*-naphth[9,10-*e*]-1,3-oxazines were also achieved.

PREFACE

The following thesis is concerned with the development of new synthetic routes to novel oxazine derivatives which are of potential photochromic importance. By way of introduction, Chapter 1 provides a survey of photochromism and photochromic materials. This is followed in Chapters 2 and 3 by an account of the results obtained in the present studies.

CHAPTER 1

A SURVEY OF PHOTOCHROMISM AND PHOTOCHROMIC MATERIALS



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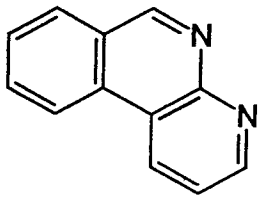

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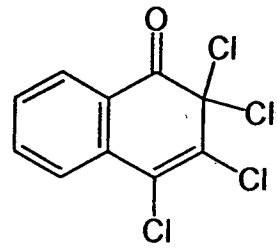

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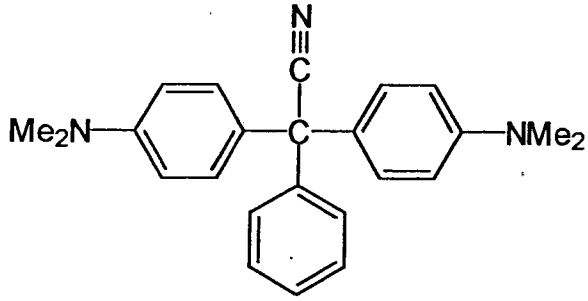


(4)

Scheme 1

1. A SURVEY OF PHOTOCHROMISM AND PHOTOCHROMIC MATERIALS

1.1 Introduction

The purpose of the following survey is to define the phenomenon of photochromism[1-3] and to describe the development of the field of photochromism from its initial discovery[4] through to recent developments. The nature of photochromism is discussed in detail and a brief overview of research in the field is given in which compounds are grouped according to the reaction mechanism responsible for their photochromic behaviour. An account is then given of some of the numerous applications[5-10] of photochromic materials in science and engineering. Potential applications requiring the development of more robust photochromic molecules are also discussed.

1.2 Photochromism: A Historical Overview

The phenomenon of photochromism was first described by Fritsche[4] in 1867. He observed (Scheme 1) that tetracene (1), an orange solid, became colourless on exposure to light and air but regained its orange colour on heating. Another early report of photochromic behaviour was by ter Meer[4] in 1876 who described a colour change in the potassium salt of dinitromethane when it was exposed to exciting radiation. Another early contributor to the field

of photochromism was Phipson[4] who observed that paint used on a gate post was black during the day but white at night. Described by the manufacturer as a 'new pigment having a zinc basis' the paint was probably similar in composition to the inorganic pigment lithopone which is a composite of barium sulphate and zinc sulphide. It is likely that fluorescent and phosphorescent effects known to be exhibited by zinc sulphide containing pigments were responsible for the photochromic behaviour observed by Phipson.

In an important early study Marckwald[4] first recognised that photochromism was a new phenomenon and described it as a truly reversible photo-reaction. In his study in 1899 he described how benzo-1-naphthyridine (2) and tetrachloro-1,2-ketonaphthalenone (3) changed colour on exposure to light with the reverse process occurring in the dark. Marckwald's name for this phenomenon was phototropy (ie to turn toward light), the term photochromism (literally coloration by light) was suggested some fifty years later by Hirschberg.[4] Other significant advances before 1900 include Wislicenus' observation[4] of the photochromism of benzalphenylhydrazone and that of certain osazones.

During the first two decades of this century most research in the field was carried out in India and Italy. Studies from this period were primarily concerned with the synthesis of new photochromic materials and observations on the type of exciting radiation required, the speed of excitation and the speed of decay and fatigue. Little information was available on the mechanism of the

photochromic processes involved. The publication of the first review article[11] on photochromism in 1929 stimulated further research in the field during the 1930's including Harris'[12] work on the mechanism of the photochromism of malachite green leucocyanide (4) and the work of Gheorghiu[13-15] on the photochromism of semicarbazones.

Since 1940 the study of photochromism has culminated in its exploitation as a scientifically and technologically important phenomenon. Many novel organic and inorganic photochromic molecules have been prepared and modern investigative techniques such as ir, nmr and esr spectroscopy and X-ray crystallography have enabled the structures of these novel compounds to be determined and the mechanisms of their photochromic behaviour elucidated. The first conference on photochromism was held in the sixties and since 1993, two international symposia have been attended by researchers from industrial and academic laboratories representing diverse fields of science and technology. The study of photochromism since its discovery can be charted through a number of review articles on the subject.[1-3,10,16,17]

1.3 The Nature of Photochromism

Photochromism is defined as a reversible change of a single chemical species between two states whose absorption spectra are distinguishably different, such a change being induced in at least one direction by electromagnetic

radiation. Thus (Figure 1), irradiation of photochromic compound (A)

$$(A)\ (\lambda_1) \underset{h\nu_2}{\overset{h\nu_1}{\rightleftharpoons}} (B)\ (\lambda_2)$$

Figure 1

gives the photoproduct (B). On removal of the exciting radiation, the photoproduct (B) reverts to its original state, the photochromic compound (A). In most cases the change in one direction is thermally induced and usually occurs spontaneously. In some cases, reversion of the photoproduct (B) to its original form (A) occurs only on exposure to electromagnetic radiation of a different wavelength. Almost all early reports of photochromism were observations of the effects of sunlight. However, it should be noted that photochromic behaviour may be initiated by electromagnetic radiation of any wavelength. The typical patterns of the absorbance prior to, during and after irradiation of a photochromic molecule are shown in Figure 2.

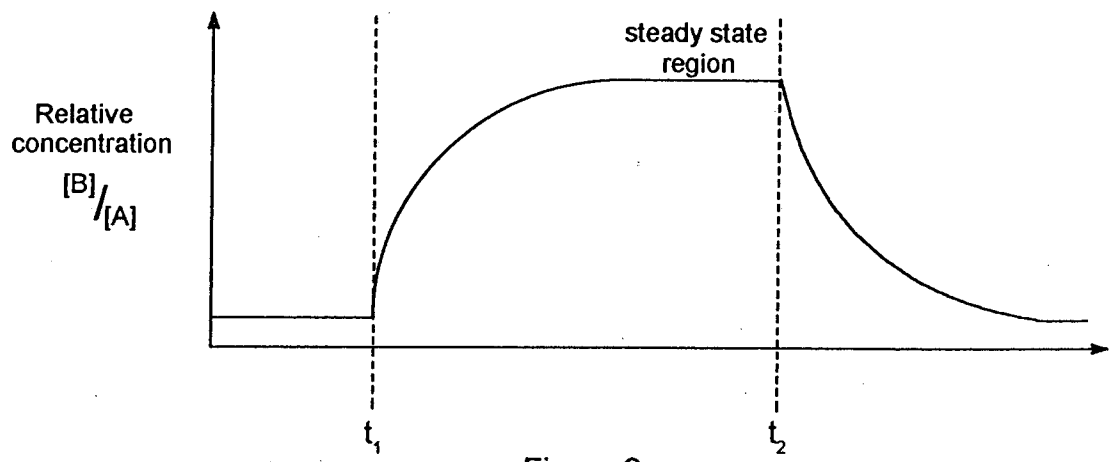
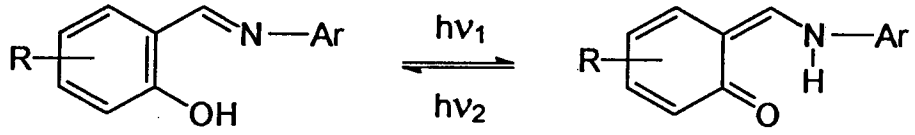


Figure 2

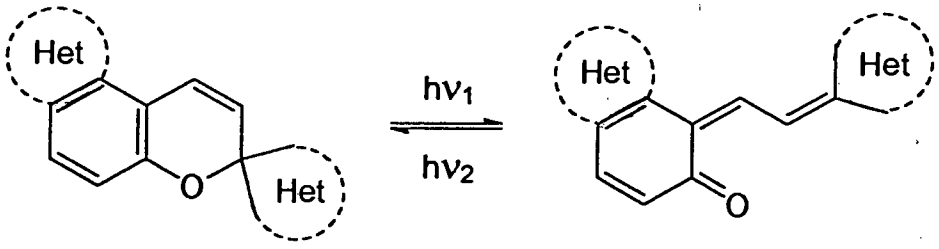


(5)

enol form
(less coloured)

(6)

keto form
(more coloured)



(7)

ring-closed form
(more coloured)

(8)

open-chain form
(less coloured)

(Ar = aromatic nucleus)
(Het = aromatic or heteroaromatic nucleus)

Scheme 2

When photochromic material (A) is irradiated at t_1 with inducing radiation hν, the concentration of the thermodynamically less stable form (B) increases with time until a steady state is reached. Following the removal of the radiation at t_2, the concentration of (B) decreases at a rate dependent on the kinetics of the reverse 'dark reaction'. Each quantum absorbed by (A) creates an excited molecule but all excited molecules may not undergo the conversion to (B) so the quantum yield is generally less than one. Quantum loss may be due to deactivating processes such as fluorescence, phosphorescence, conversion to heat and permanent chemical change. Irreversible photochemical reactions are a threat to the lifetime of a photochromic material which for practical purposes must be capable of prolonged reversible photochromic behaviour. This loss of reversibility is termed fatigue. Resistance to fatigue is one of the most important properties of a photochromic system. Other important properties include the absorption wavelengths and extinction coefficients of the photochromic compound and its photoproduct and the effect of environmental factors such as solvent and temperature.

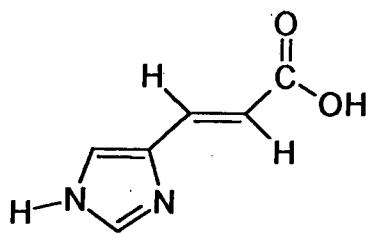
The majority of photochromic processes are unimolecular. The photochromic species (A) may be a molecule or ion whereas the thermodynamically less stable photoproduct (B) may be a single species or a number of species the recombination of which gives (A). For example (Scheme 2), (A) can be the phenolic (enol) form (5) of an anil of salicylaldehyde where the photoproduct (B) is the less stable keto form (6). In this case, as in many photochromic systems the thermodynamically less stable form (B) [ie (6)] is the more deeply

coloured. Hence, the observed effect is a colourless material becoming coloured on irradiation. However, the more stable form (7) of certain spiropyrans is known to exhibit a deeper colour than their open-chain photoproducts (8). In such cases the forward reaction is known as photobleaching. It should be noted that photochromic processes involving colour changes, for example yellow to red are also known.[18] In such systems a shift of the absorption spectrum towards the blue region is known as a hypsochromic shift while a shift towards the red region of the spectrum is called a bathochromic shift

1.4 Photochromic Systems

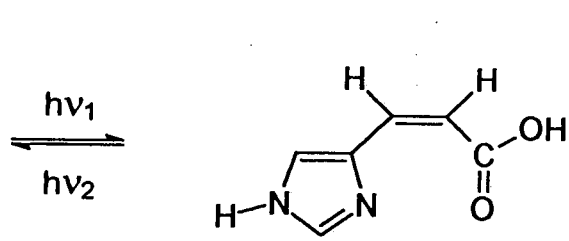
Since Fritsche[4] first described the phenomenon of photochromism a large number of photochromic compounds have been synthesised. The following account describes some of the more important types classified according to the mechanism of the photochromic processes involved. The main types of photochromic processes are based on *cis-trans* isomerisation, pericyclic reactions, tautomerism and dissociation processes.

The interconversion of the *cis* and *trans* isomers of alkenes by photoinduced 180°C rotation about the carbon - carbon double bond is a well understood



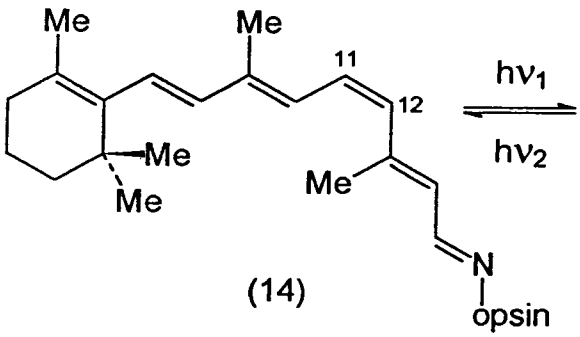
(trans)

(12)



(cis)

(13)



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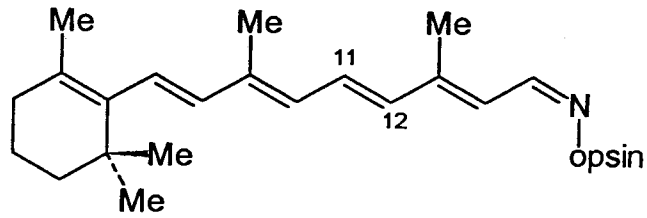
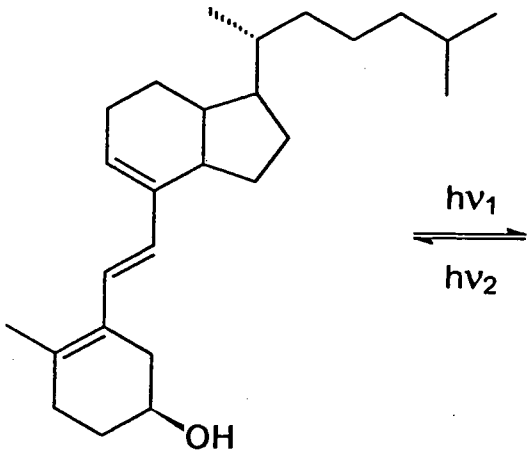


(15)



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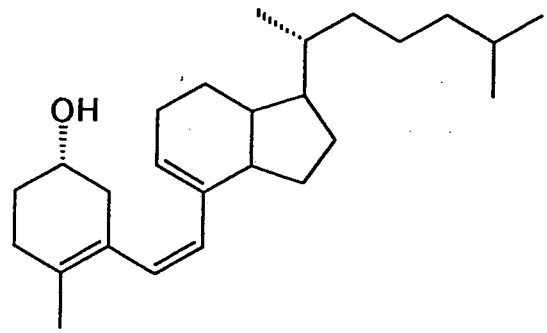
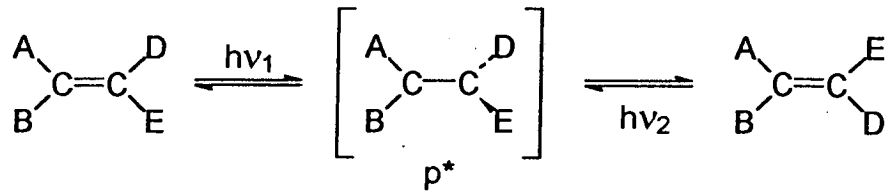


(17)

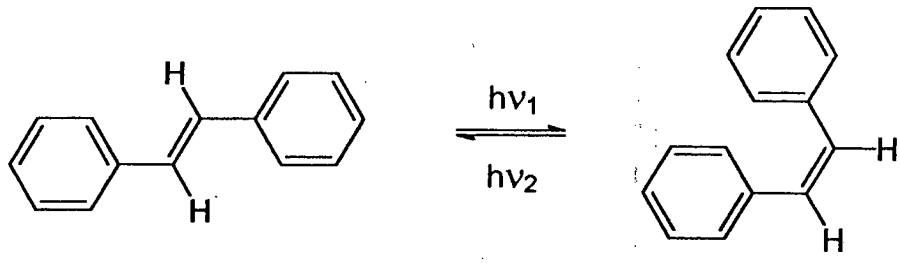
Scheme 4



(9) (10) (11)

Scheme 3

process. Excitation (Scheme 3) of an alkene (9) substantially reduces the bond order of the olefinic carbon-carbon bond. The excited alkene relaxes by twisting to a perpendicular or phantom excited state (p*) (10). Radiationless decay from the p* state (10) gives either the starting alkene (9) or the isomeric product (11). This type of process is often photochromic as the two isomers usually have different absorption spectra. Such photoisomerisations are well known in naturally occurring alkenes. For example (Scheme 4), the photochromic behaviour of uranoic acid is due to photoinduced interconversion of its *cis* (12) and *trans* (13) isomers. The process is believed to be the mechanism involved in the dissipation of harmful ultraviolet radiation by the epidermis.[19] The first step of the mechanism by which the retina detects light is also a photoinduced *cis-trans* isomerisation.[19] Rhodopsin (14), the Schiff base of 11-*cis*-retinal with the protein opsin, is photoisomerised to the all-*trans* isomer prelumirhodopsin (15). The interconversion of tachysterol (16) and previtamin D (17), a step in the biosynthesis of vitamin D also involves a photoinduced isomerisation about an olefinic bond.[19]

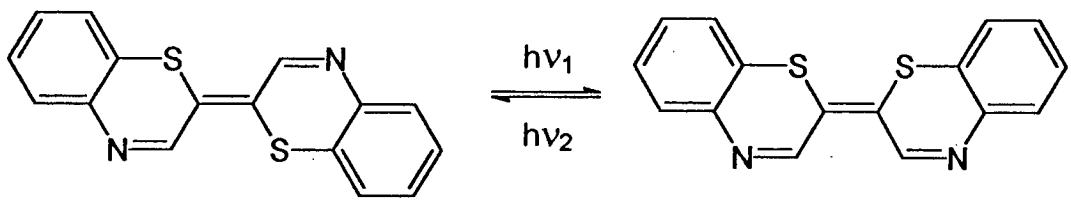


(*trans*)

(18)

(*cis*)

(19)

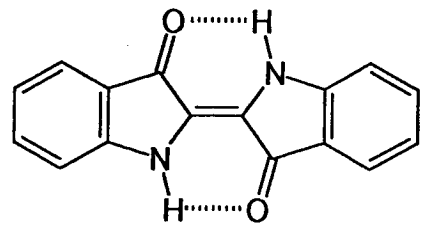


(*trans*)

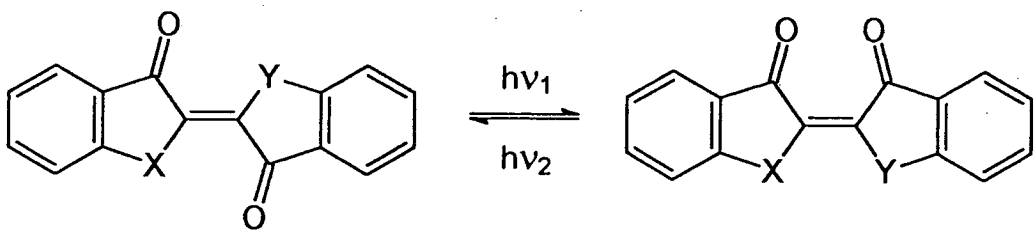
(20)

(*cis*)

(21)



(22)



(*trans*)

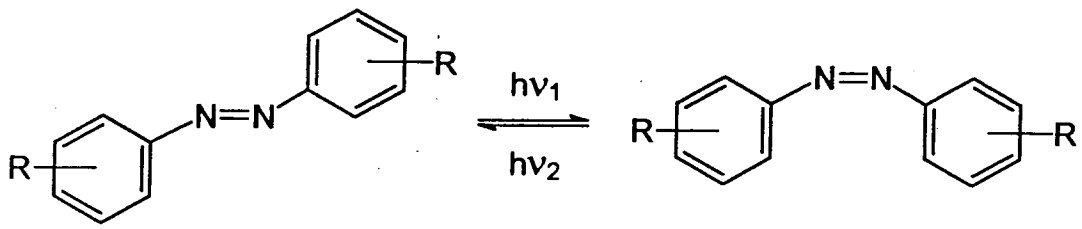
(23)

(*cis*)

(24)

(X, Y = S, Se, O, NR)

Scheme 5

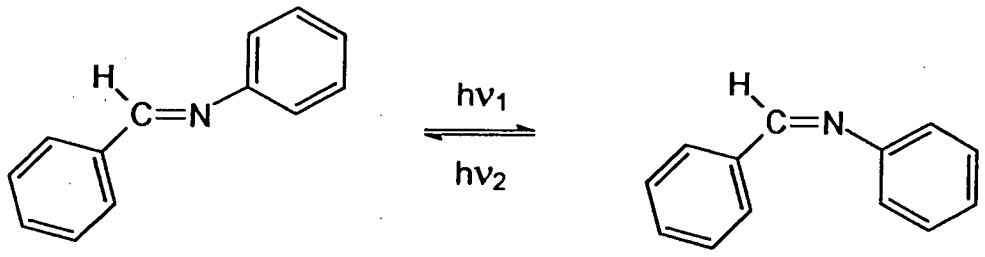


(*E*)

(25)

(*Z*)

(26)



(anti)

(27)

(syn)

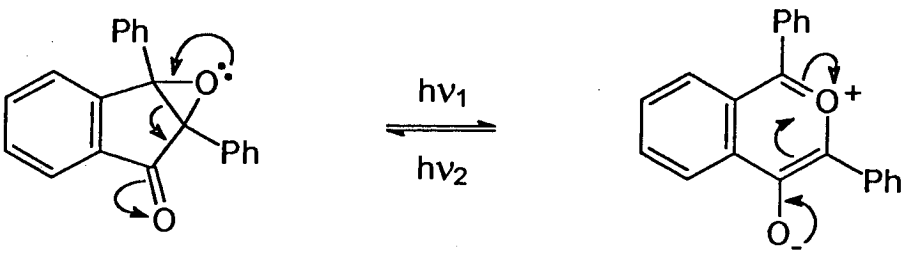
(28)

Scheme 6

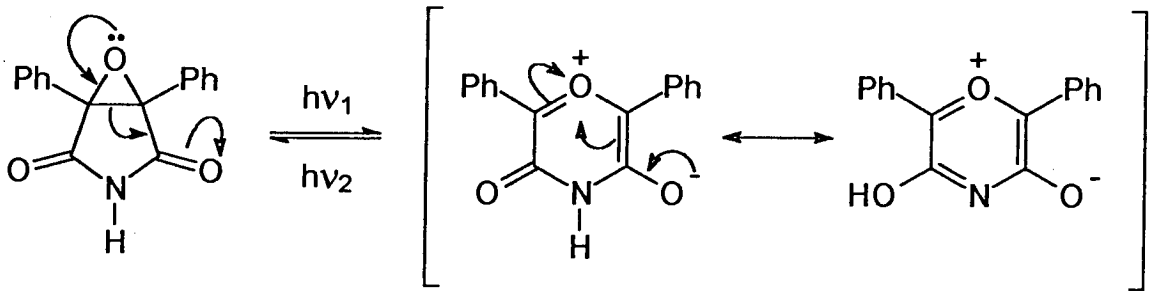
The reversible *cis-trans* isomerisation (Scheme 5) of stilbenes [(18) ⇌ (19)] is also a photochromic process which has been the subject of many investigations.[19-22] Similarly, irradiation of the yellow *trans* isomer (20) of $\Delta^{2,2'}$-bi-(2*H*-1,4-benzothiazine)[18] causes isomerisation to the red *cis* isomer (21). The reverse reaction can be induced thermally or photochemically.[23] The dyestuff indigo (22) which consists of two indoline rings linked by a central olefinic bond is incapable of isomerisation about the double bond due to hydrogen bonding between the NH and carbonyl functionalities.[24] However, (Scheme 5) several indigoid compounds which do exist in *trans* (23) and *cis* (24) forms have been reported in the literature. The heteroatoms X and Y can be sulphur,[25] selenium,[26,27] oxygen[28] or nitrogen.[29,30] Providing neither X or Y is NH, indigoids of this type exhibit photochromic behaviour due to geometric isomerisation about the central carbon-carbon double bond.

The azo group is isosteric with the ethylene group and therefore aromatic azo compounds (Scheme 6) also exhibit photochromism due to reversible photoisomerism between *E* (25) and *Z* (26) forms. Among the many examples reported in the literature[19,20,31,32] are azo compounds whose aromatic rings have been functionalised with polymerisable side chains and crown ethers.[32]

The search for Schiff bases which exhibit photochromism by *syn-anti* isomerism about the carbon-nitrogen double bond has been much less fruitful than systems based on photoisomerism of carbon-carbon double bonds or azo functionalities. Benzylideneaniline has been shown (Scheme 6) to exhibit

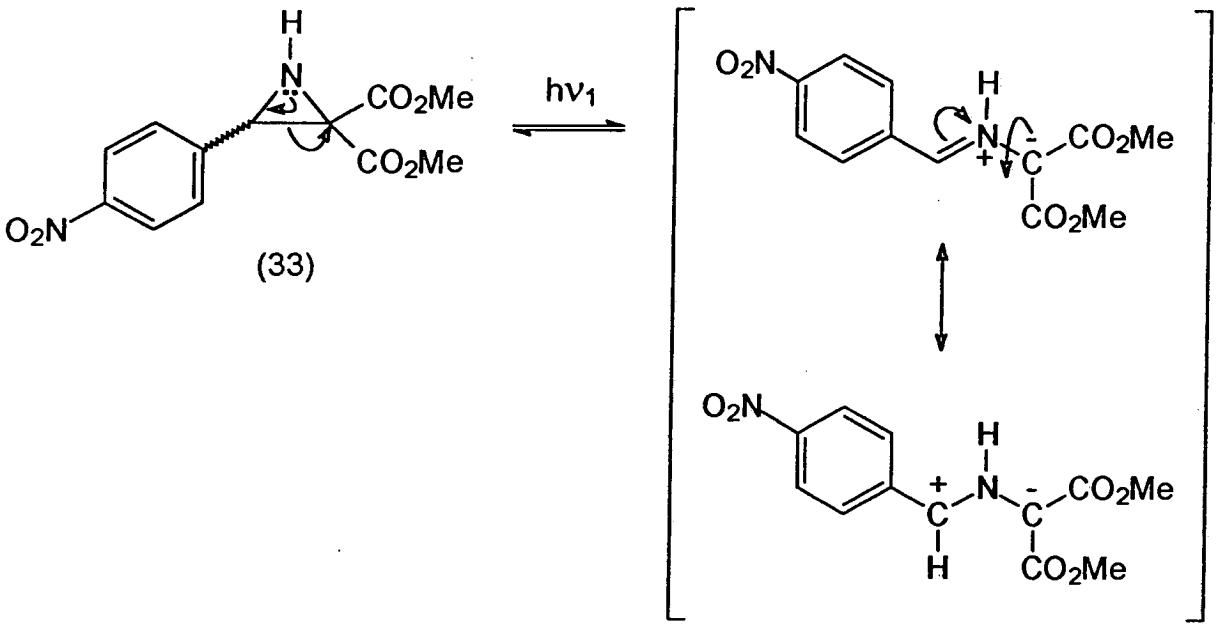


(29) (30)

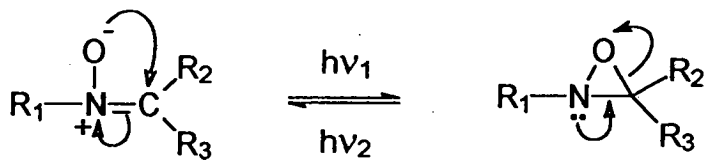


(31) (32)

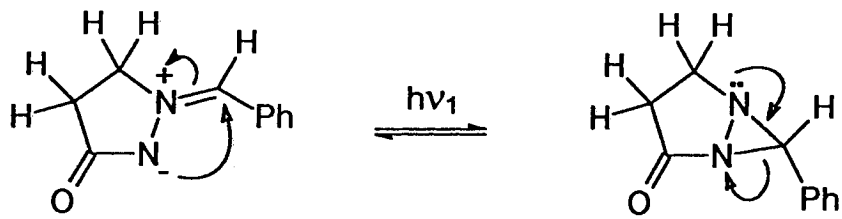
Scheme 7



(33) (34)



(35) (36)

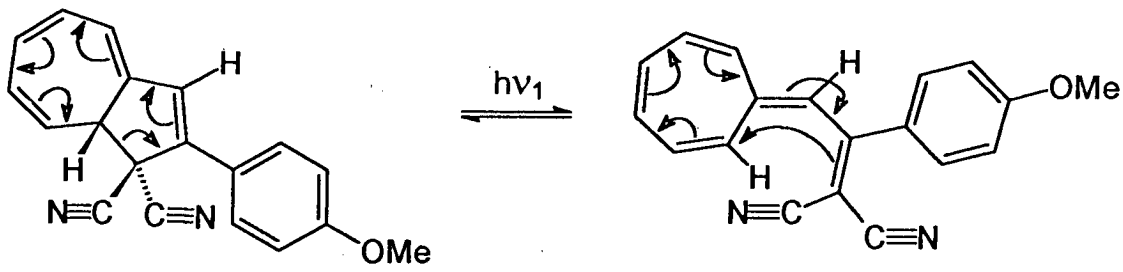


(37) (38)

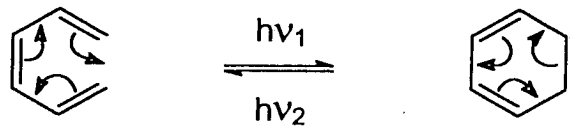
Scheme 8

reversible photochemical change at low temperature which Fischer and Frei suggest to be due to *anti* (27) - *syn* (28) isomerism at the carbon-nitrogen double bond.[33] It should be noted that many examples of photochromic Schiff bases are known [see Page 13, Scheme 15; (73)] but their photochromism is due to tautomerism and will be discussed later in this chapter.

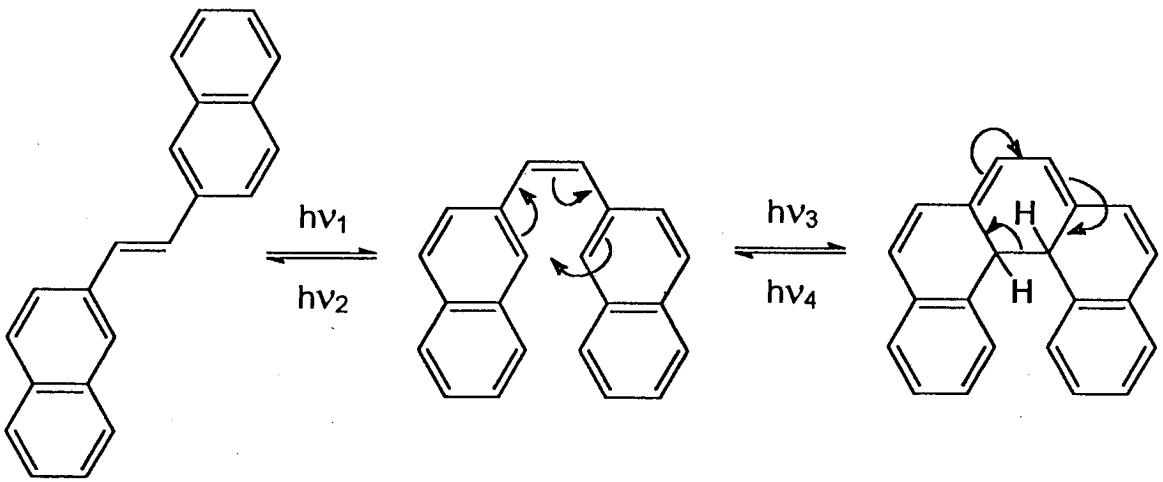
There are many examples of photochromic behaviour due to electrocyclic processes and in particular electrocyclic ring closure which involves the formation of a new σ-bond between the terminal atoms of a conjugated π-system. Electrocyclic ring opening is the reverse of this and when the cyclic and ring-opened forms have different absorption spectra the process is by definition photochromic. Certain epoxides exhibit photochromism due to electrocyclic processes. For example (Scheme 7), the indenone oxide derivative (29) undergoes electrocyclic ring-opening on irradiation.[34] The resulting highly coloured diphenylbenzopyrylium oxide (30) can be photochemically bleached regenerating the indenone oxide (29). Similarly, (Scheme 7) the colourless epoxydiphenylsuccinimide (31) undergoes photoinduced electrocyclic ring opening to give the coloured ylide (32).[35] As the process is reversible by irradiation with light of a different wavelength the process is photochromic. Photochromic molecules containing an aziridine nucleus have also been described.[36-39] Recent work by Schirmeister[39] (Scheme 8) described the synthesis and photochromism of the aziridine-2,2-dicarboxylate derivative (33) which reversibly photoisomerises to give the deep red azomethine ylide (34). In photochromic processes involving oxaziridene



(39) (40)

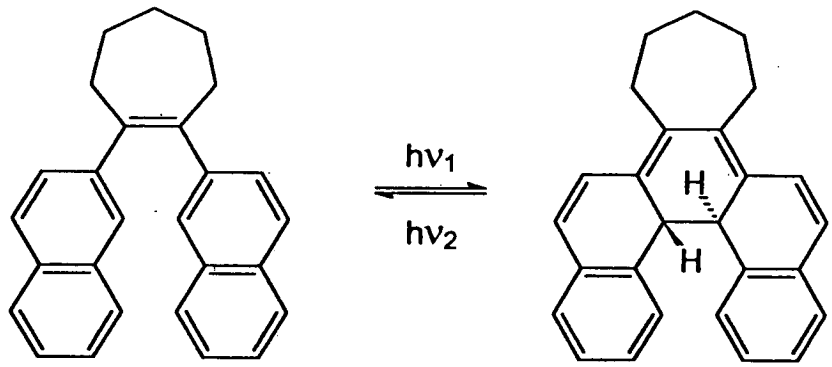


(41) (42)

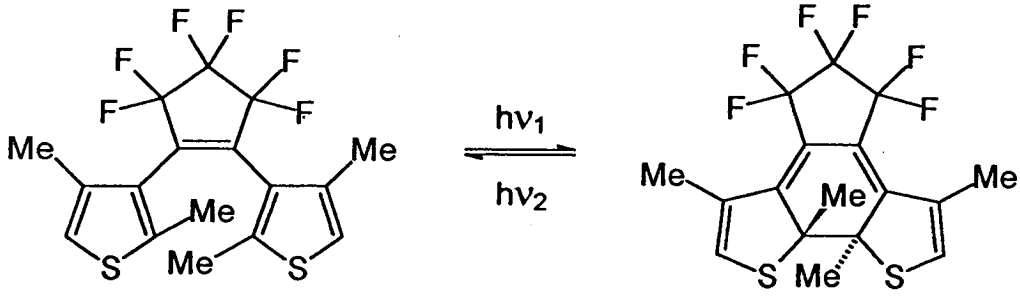


(43) (44) (45)

Scheme 9

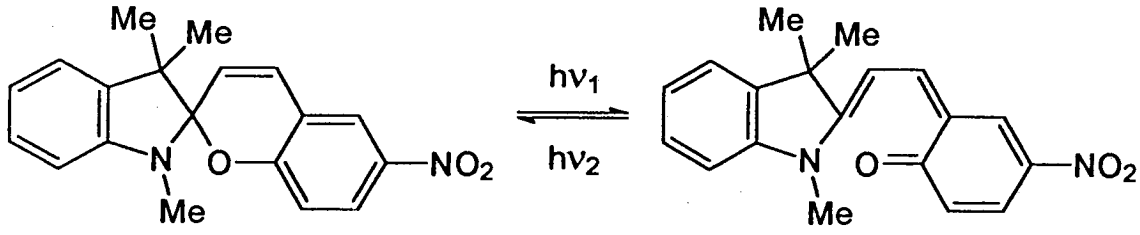


(46) (47)



(48) (49)

Scheme 10



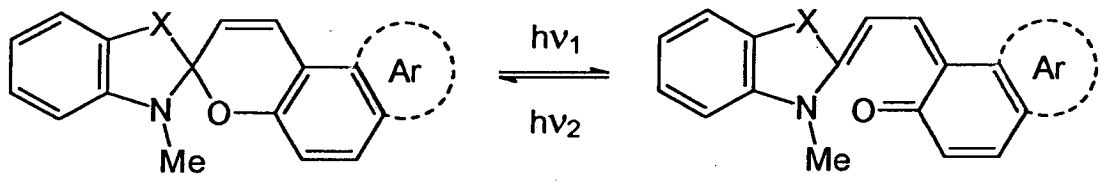
(50) (51)

Scheme 11

ring systems (36) it is usually the ring-opened nitrone form (35) which is more thermodynamically stable.[40] Oxaziridines (36) are prone to irreversible side reactions and therefore must be stabilised by appropriate substituents. An example of a photochromic system (Scheme 8) based on a diaziridine nucleus is the bicyclic compound (38),[38] the most stable form of which is the azomethine imine (37). Irradiation of the azomethineimine (37) causes reversible photoisomerisation to the diaziridine (38) while the back reaction is thermally initiated.[38]

Photochromism due to electrocyclic rearrangement is also illustrated (Scheme 9) by the photoisomerisation of the yellow dihydroazulene derivative (39) to the dark red 8-vinylheptafulvene derivative (40).[41] The dihydroazulene derivative (39) is regenerated following electrocyclic ring-closure of the photoproduct (40) which occurs on removal of the light source.

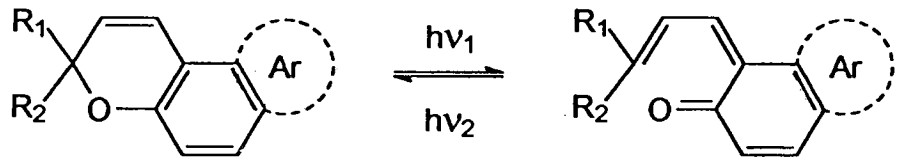
Several photochromic systems based on the electrocyclic interconversion of *cis*-hexa-1,3,5-triene (41) and cyclohexa-1,3-diene (42) have been reported.[42] A simple example is the reversible electrocyclisation of *cis*-1,2-dinaphth-2-ylethene (44) to the dibenzodihydrophenanthrene derivative (45).[43] The *cis* isomer (44) is structurally analogous to the previously discussed *cis*-stilbene [see Page 7, Scheme 5; (19)] and therefore exhibits photoinduced isomerisation (Scheme 9) to the *trans* form (43) in competition with electrocyclisation to the ring-closed form (45).[43] To exclude the competing geometric isomerisation (Scheme 10) compounds such as 1,2-dinaphth-2-



X
a; O
b; S
c; Se

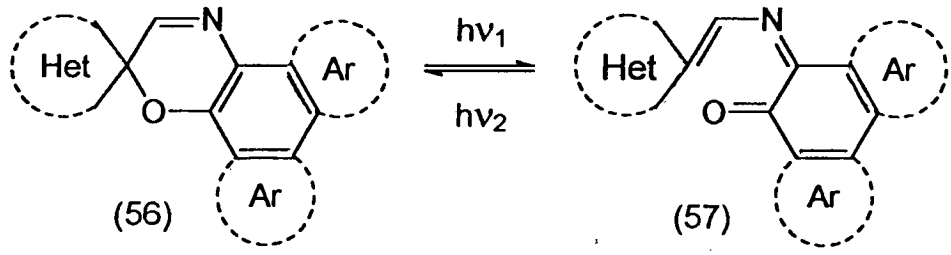
(52) (53)

(Ar = aromatic nucleus)

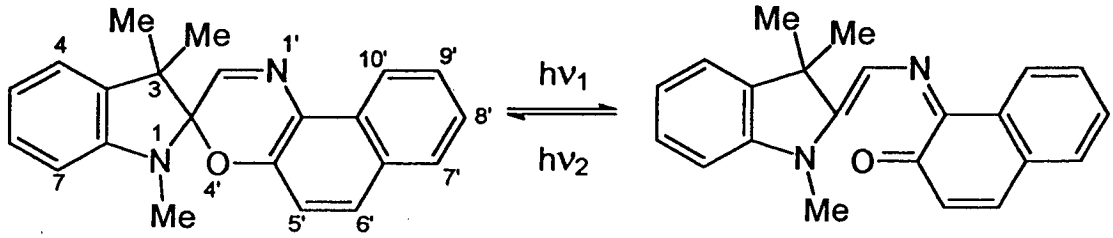


(54) (55)

(Ar = aromatic or heteroaromatic nucleus) (Het = heteroaromatic nucleus)



(56) (57)



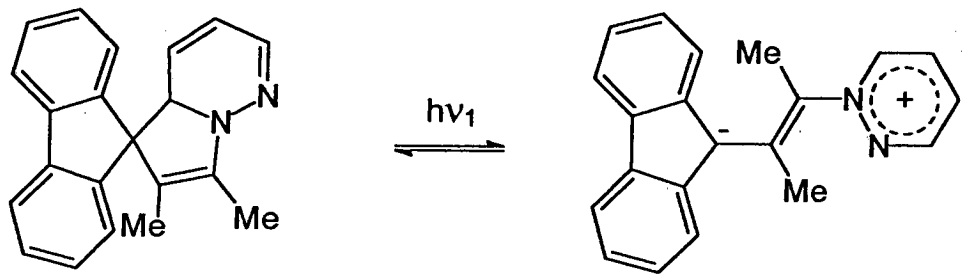
(58) (59)

Scheme 12

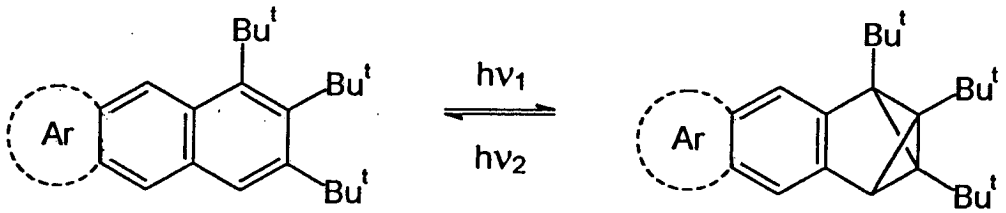
ylcycloheptene (46) have been prepared[44] where the naphthalene rings are locked in a *cis* orientation with respect to the central double bond. Electrocyclic ring-closure of (46) affords the photoproduct (47) whose absorption spectrum is bathochromically shifted. Many analogous compounds functionalised with heterocyclic rings have been prepared[45-48] including 1,2-bis-(2,4-dimethylthien-3-yl)perfluorocycloheptene (48) whose electrocyclisation to the ring-closed form (49) is a highly fatigue resistant process.[47]

Since their photochromism was first reported by Hirshberg[48] in 1952, spiropyrans (Scheme 11) have been the subject of a large number of publications and patents.[37,49-66] Irradiation of the ring-closed form (50) causes cleavage of a carbon-oxygen bond affording the photomerocyanine ring-opened form (51). The ring-closed form [eg (50)] is usually the least coloured. However, the reverse is true of certain spiropyrans bearing free hydroxy, carboxy or amino groups on either benzene ring.[63] The most extensively investigated benzopyrans are the indolobenzopyrans [eg (50)]. However (Scheme 12), photochromic systems based on pyrans fused to benzoxazoline (52a), benzothiazoline (52b) and benzoselenazolene (52c) rings have been reported[37,51] as have 'non-spiro' 2,2-disubstituted 2*H*-benzopyrans and structurally related condensed systems (54).[67,68]

Since the synthesis and photochromism of certain spirooxazine derivatives was first reported in 1961,[69] there has been much interest in these fatigue resistant compounds,[69-82] which undergo the electrocyclic ring opening generalised in

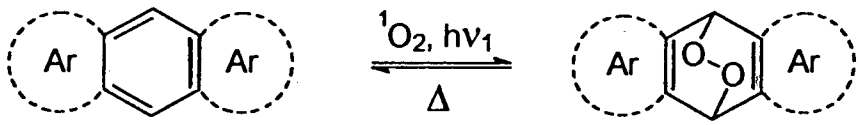


(60) (61)



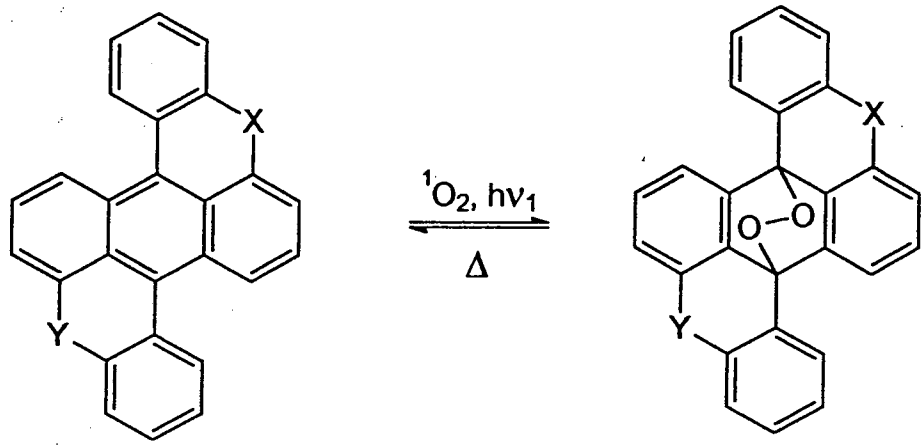
(62) (63)

Scheme 13

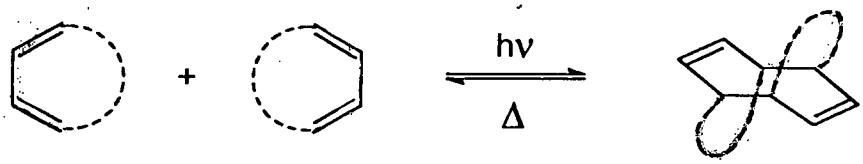


(64) (65)

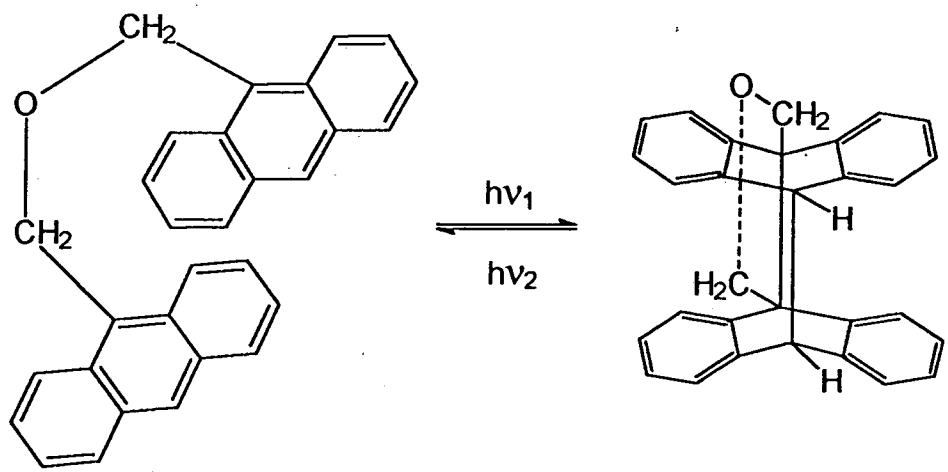
(Ar = aromatic nucleus)



(66) (X,Y = O, S, NPh) (67)



(68) (69) (70)



(71) (72)

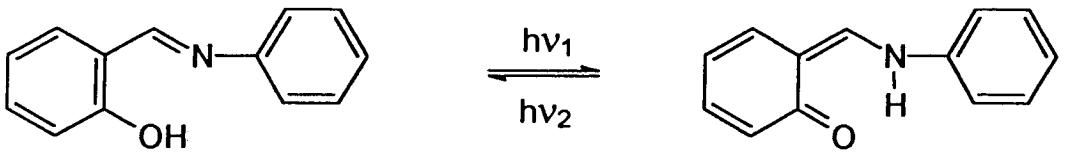
Scheme 14

[Scheme 12; (56) ⇌ (57)]. A typical example is the 1,3,3-trimethylspiro[indoline-2,3'-[3*H*]naphth[2,1-*b*]-1,4-oxazine] (58) which undergoes electrocyclic ring-opening to give the blue merocyanine dye form (59) under ultraviolet irradiation.[69]

A further class of compounds which owe their photochromism to an electrocyclic process (Scheme 13) is the dihydroindolizines.[82-85] On irradiation, the spirofluorenyldihydroindolizine (60) undergoes electrocyclic ring opening of the azacyclopentene ring to give the coloured betaine (61) which spontaneously cyclises on removal of the light source to regenerate the dihydroindolizine (60).

Certain sterically crowded aromatic compounds (62) have recently been reported[86] to undergo a reversible photoinduced electrocyclic rearrangement to give valene-type isomers (63). As the product of this valence isomerisation (63) has an absorption spectrum different to that of the fully aromatic starting compound (62) the process is photochromic.

Cycloadditions are another important class of reactions which provide the basis for photochromic systems. The [4+2] cycloaddition of singlet oxygen to aromatic compounds is a highly efficient photochromic process.[87] Such photooxygenation (Scheme 14) of an aromatic compound (64) gives an endoperoxide (65). The reversible photobleaching of tetracene [see Page 1, Scheme 1; (1)] first observed by Fritsche[4] involves such photo-oxygenation.

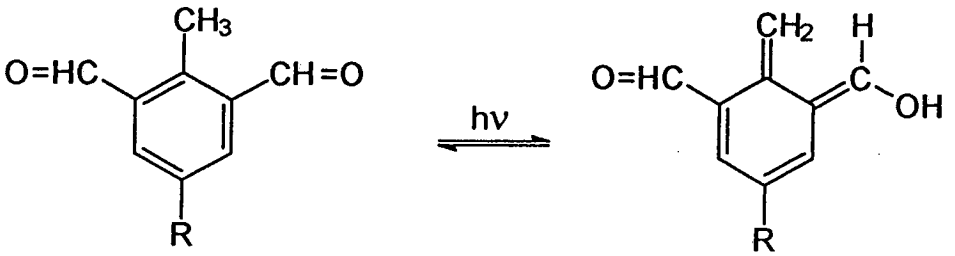


(enol tautomer)

(73)

(keto tautomer)

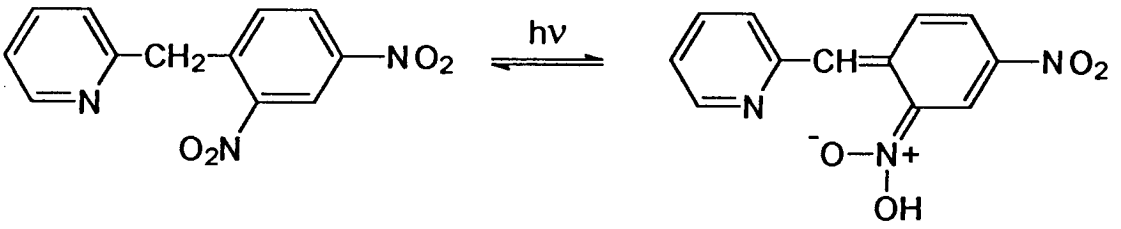
(74)



(75)

(76)

(R = Me or Pr^i)

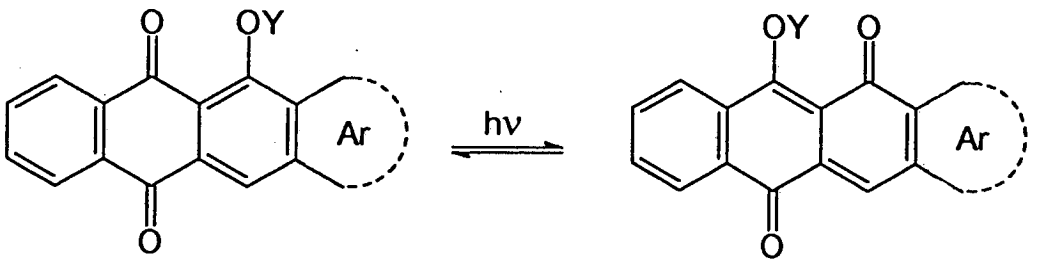


(nitro tautomer)

(77)

(aci-nitro tautomer)

(78)



(79)

(80)

Y

a; CO.R

b; Ph

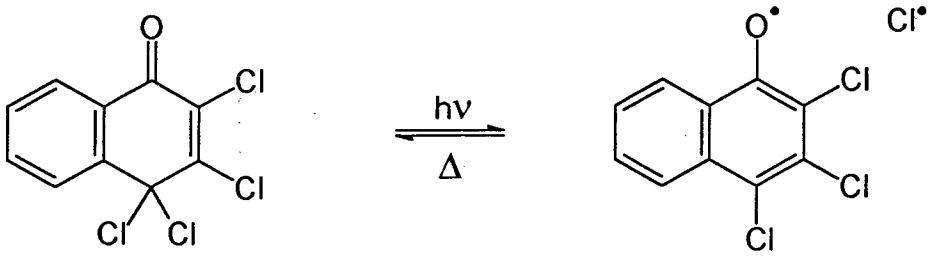
(Ar = aromatic nucleus)

Scheme 15

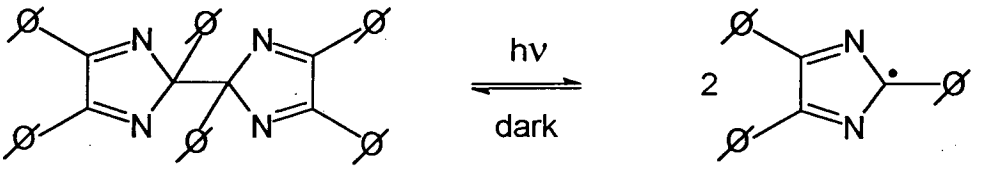
Recently reported[88] aromatics exhibiting photochromism due to this type of process include heterocyclic analogues of benzodixanthene (66). The coloured compounds (66) become colourless on photo-oxygenation to the endoperoxide adducts (67).

[4+4] Cycloadditions are a much studied group of photochemical reactions[89] which can be formally depicted as in [Scheme 14; (68) + (69) $\rightleftharpoons$ (70)]. The cycloisomerisation of the bisanthrene derivative (71) to the photoproduct (72) was first reported by Bouas-Laurent *et al.*[90] They suggested that this process mimics the opening and closing of a jaw and named such compounds 'jaw photochromics'. Photochromic compounds of this type have been the subject of further studies[89,91,92] since they were first reported.[90]

Tautomerism is also a source of photochromic behaviour. Photochromic tautomerism is defined as a photochemically induced shift in the equilibrium between tautomers which have significantly different absorption spectra. The hydrogen transfer tautomerism exhibited by certain anils of salicylaldehyde derivatives has been the subject of several studies.[93,59] For example (Scheme 15), the pale yellow phenolic (enol) form of the salicylaldehyde anil (73) is the more thermodynamically stable form. Irradiation of the phenolic form (73) initiates a reversible proton transfer giving the red keto form (74).[93] A more recently discovered example of photochromic tautomerism is the reversible photoenolisation of certain alkylisophthalaldehydes.[96] Irradiation of the colourless alkylisophthalaldehyde (75) gives the red enol form (76) which in



(81) (82)



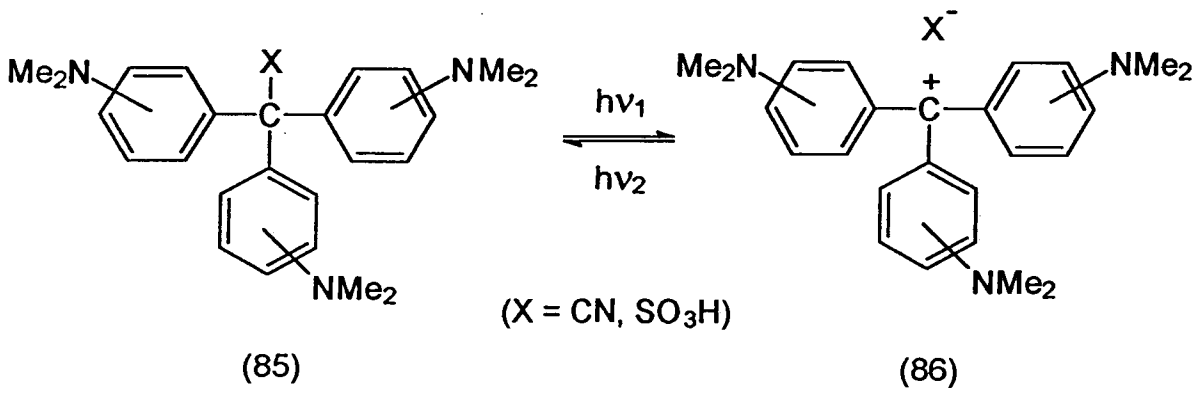
(83) (84)

Scheme 16

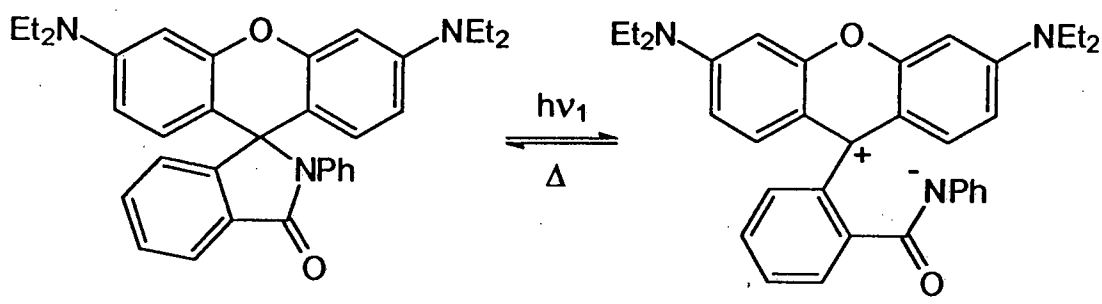
turn reverts to the dialdehyde (75) on removal of the light source. The photochromism of 2-(2,4-dinitrobenzyl)pyridine (77) was well known[97,98] before the reversible prototropic tautomerism responsible for this phenomenon was described.[97,99] Irradiation of the thermodynamically more stable nitro form (77) affords the coloured aci-nitro tautomer (78) whose absorption spectrum is bathochromically shifted with respect to the starting tautomer (77).

The photochromism exhibited by certain substituted quinones is shown in general form in (Scheme 15). Such photochromism is due to the reversible isomerisation of the para-quinone form (79) to the highly coloured ana-quinone form (80).[100-103] The photoinduced acyl migration [(79a)→(80a)] is thermally reversible while the analogous aryl migration [(79b)→(80b)] can only be reversed photochemically.[100]

Photochromic systems involving homolytic cleavage of N-N,[104] C-C,[105] C-Cl,[105] and S-S,[106] bonds are known. For example (Scheme 16), photochromism is observed due to the reversible photodissociation of a chlorine atom from the naphthalene derivative (81) giving the highly coloured photoproduct (82). The reverse process, the thermal reformation of a carbon-chlorine bond, regenerates the ketone (81). Irradiation of a benzene solution of the bis-imidazole (83) causes a colour change from yellow to reddish-purple with the original colour returning in the dark.[105] The reddish-purple colour is believed to be due to the radical species (84). The generation of such radical species



(85) (86)



(87) (88)

Scheme 17

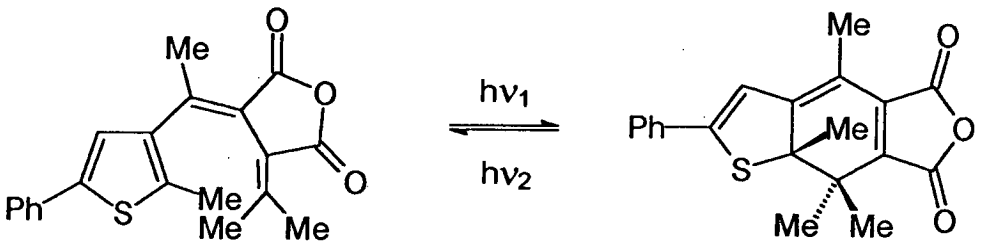
in photochromic processes involving homolytic cleavage renders such systems vulnerable to side reactions resulting in rapid fatigue.

Photochromism associated with heterolytic bond cleavage[37] is exhibited by several triarylmethane derivatives (Scheme 17). Irradiation of colourless triarylmethane derivatives (85) results in heterolytic bond cleavage and formation of highly coloured triarylmethane cations (86) which recombine with the anion in the reverse process. Several compounds structurally closely related to triarylmethane dyes have also been found to exhibit photochromism.[37] For example, the rhodamine derivative (87) undergoes photoinduced carbon-nitrogen bond cleavage to give the highly coloured photoproduct (88).[109] The rhodamine derivative (87) may be considered as a triarylmethane analogue in which the bleaching anion is built into the molecule.

1.5 Practical Applications of Photochromic Systems

The photoinduced reversible colour change exhibited by photochromic materials has resulted in their exploitation for many applications in diverse fields of science and technology.[6-10] The following account details a few such applications categorised according to the specific photochromic property utilised.

The photosensitive nature of photochromic compounds has given rise to a number of applications. For example, a photochromic species whose behaviour under known intensities of light was well characterised could then be used to determine the intensity of an unknown light source.[8] An example of this (Scheme 18) is the pale violet fulgide (91) which is converted into the deep red anhydride (92) on irradiation at 366 nm. The reverse process occurs on irradiation with visible light. Hence this process has



(pale violet)
(91)

(deep red)
(92)

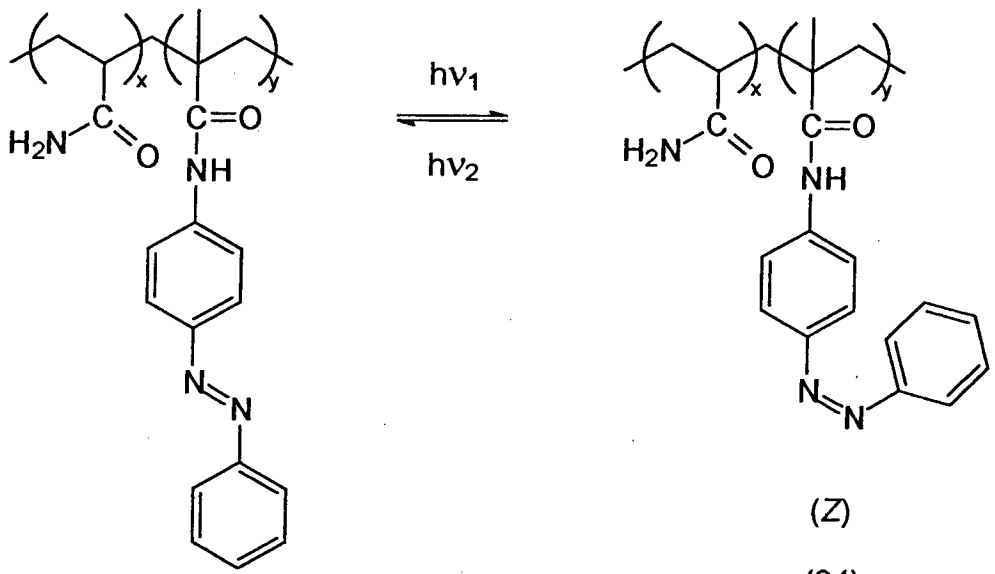
Scheme 18

been advocated as a visible light actinometer which could be easily regenerated with ultraviolet radiation.[108] To be suitable for this application the photochromic species must be thermodynamically stable in both forms. This characteristic is exhibited by many fulgides the photochromism of which has been reviewed in the literature.[108-111]

Dispersion of certain spiropyrans [see Page 11, Scheme 11; (50)] in a polyvinylchloride resin increases the stability of the open chain

photomerocyanine form (51). The stability of the coloured form (51) in this system is the basis of patents describing the use of spiropyrans in PVC resin coated on a paper support as a photographic system which requires no developing.[6,111,113]

There are also many potential applications of photochromic materials based on the specific colour change they undergo. Photochromic compounds have been used in techniques for the visualisation of fluid flow which cause no disturbance to the flow itself. Quantitative investigations of fluid flow have been carried out by the projection of ultraviolet gridlines onto a flowing solution containing a photochromic element.[113] A coloured grid becomes visible in the solution and as the solution flows the grid appears to move and the velocity of the flow can be measured. The deformation of the coloured grid gives an indication of the vorticity of the flow. The use of ultraviolet sensitive photochromic materials in bank notes as security markings which are invisible under normal illumination has been the subject of a recent study.[114] Likewise the use of a photochromic element in any security document would make the manufacture of counterfeits more difficult.[117] Photochromic cosmetics[116,117] and toys[118] have also been reported, an example of the latter being a doll which suntans! Textiles functionalised with photochromic molecules have been used for the production of novelty clothing[120] but could also find application in the manufacture of camouflage fabrics which change shade in response to changes in illumination. Similarly, photochromic paints could also find application in the camouflage of military vehicles and aircraft.



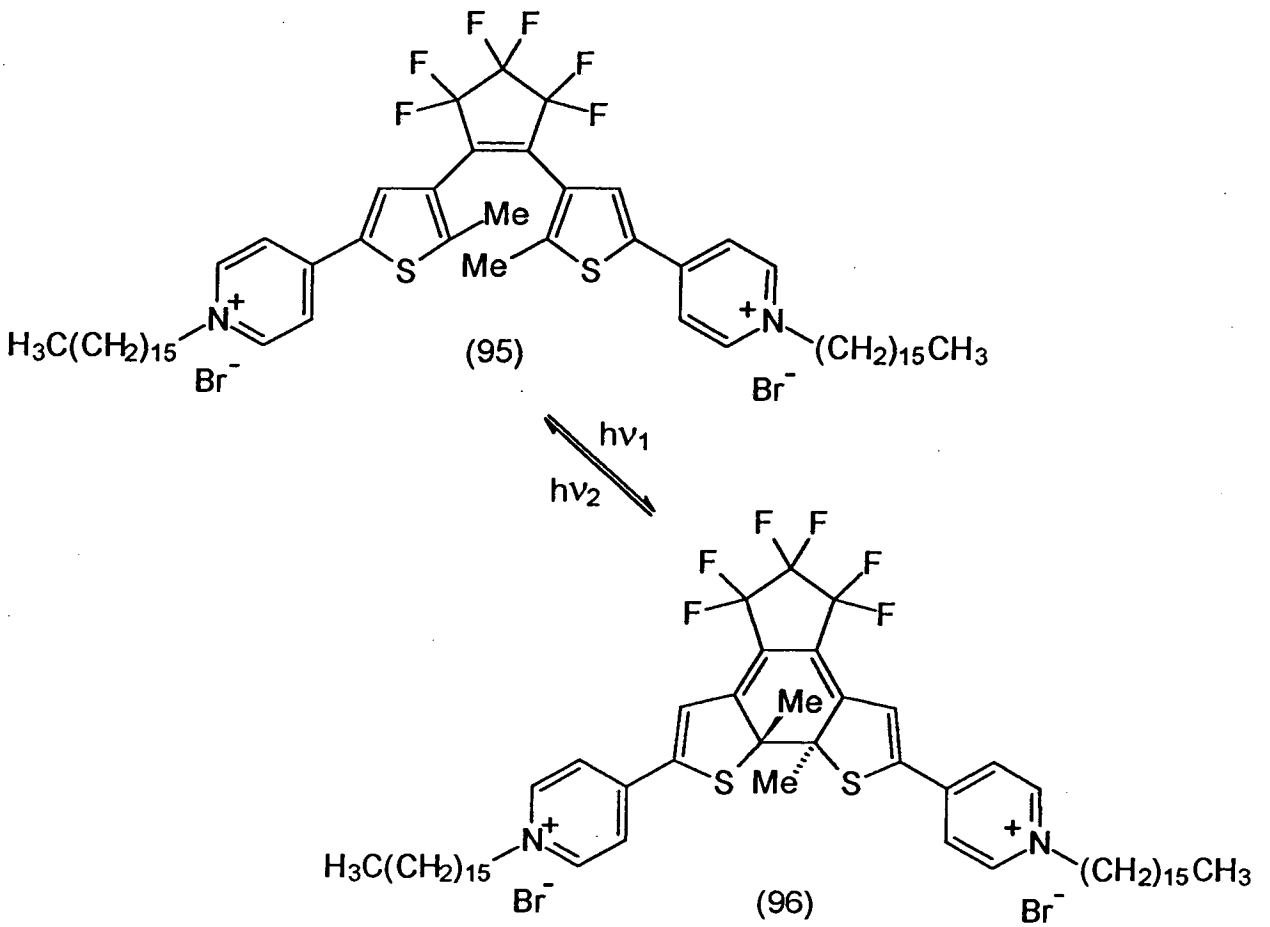
(*E*)

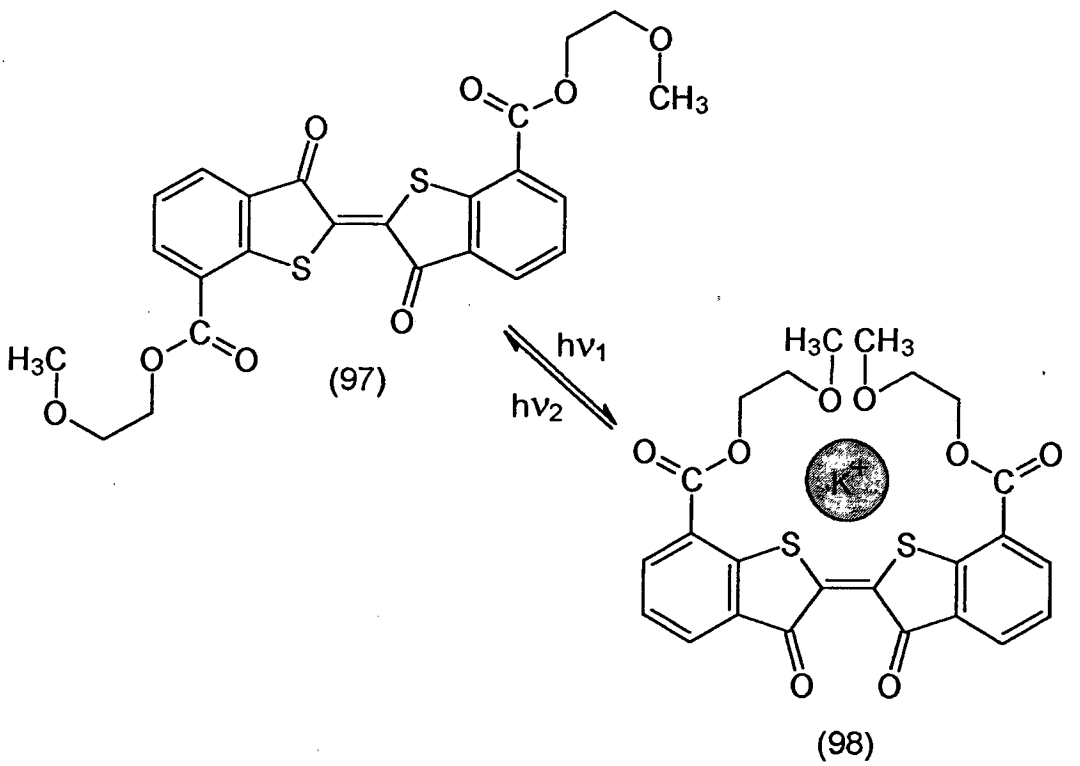
(93)

(*Z*)

(94)

Scheme 19

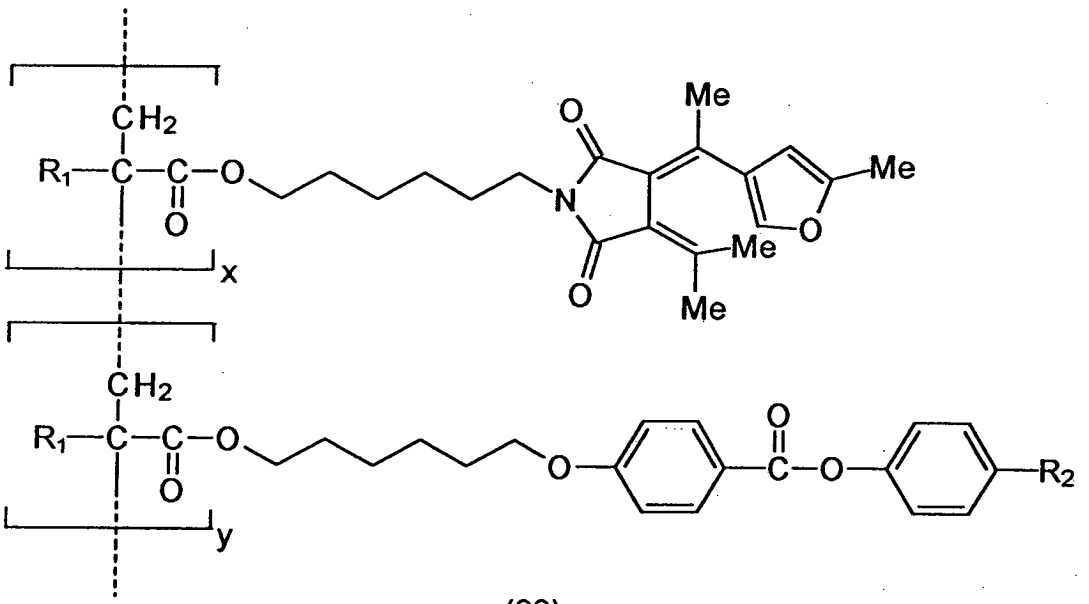

F F
F F
F F
Me
Me
S
S
N+
H3C(CH2)15
Br-
(95)
+N
(CH2)15CH3
Br-
hν1
hν2
F F
F F
F F
Me
S
Me
S
N+
H3C(CH2)15
Br-
(96)
+N
(CH2)15CH3
Br-


O
O
O
CH3
O
S
S
O
H3C
O
O
O
(97)
hν1
hν2
H3C CH3
O
O
O
O
O
K+
S
S
O
O
O
(98)

Scheme 20

There are a number of applications of photochromic compounds which take advantage of the reversible nature of the processes they undergo. The reversible changes induced in a photochromic species on irradiation are not just limited to its absorption spectrum. The coloured and colourless forms of a photochromic material may also differ in refractive index, polarity and polarisibility.[120] For example, polymers containing photochromic groups have been shown to exhibit changes in volume and viscosity on irradiation.[120] Willner and co-workers[121] report the preparation (Scheme 19) of a polymer functionalised with azobenzene side-chains which also contains an immobilised enzyme, α-chymotripsin. The authors observed that the hydrolytic activity of the immobilised enzyme was affected dramatically by the photoisomerisation of the azobenzene groups. With the azobenzene moieties in a *Z* orientation (94) the immobilised α-chymotripsin hydrolysed its substrate efficiently. Following photo-induced isomerisation of the azobenzene groups to the *E* form (93) no hydrolysis of the substrate occurred. This loss of enzyme activity is believed to be due to a change in permeability of the substrate across the polymer matrix, denying the substrate access to the enzyme.[121]

The potential for photochromic compounds to find application in the manufacture of optically triggered switches for use in the electronics industry has been known for some time.[5] Recent publications[122,123] have detailed the development of an electrode modified with diarylethene moieties (Scheme 20). Electron transfer from the modified electrode can be switched on and off photochemically. The authors claim that the change in the electrochemistry of



(99)

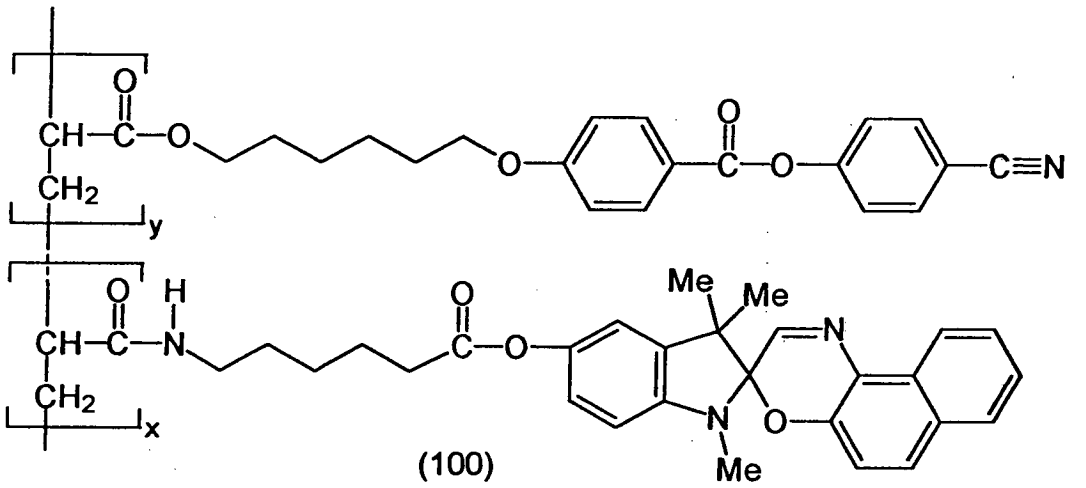
	R_1	R_2
a;	H	CN
b;	CH_3	OMe

Scheme 21

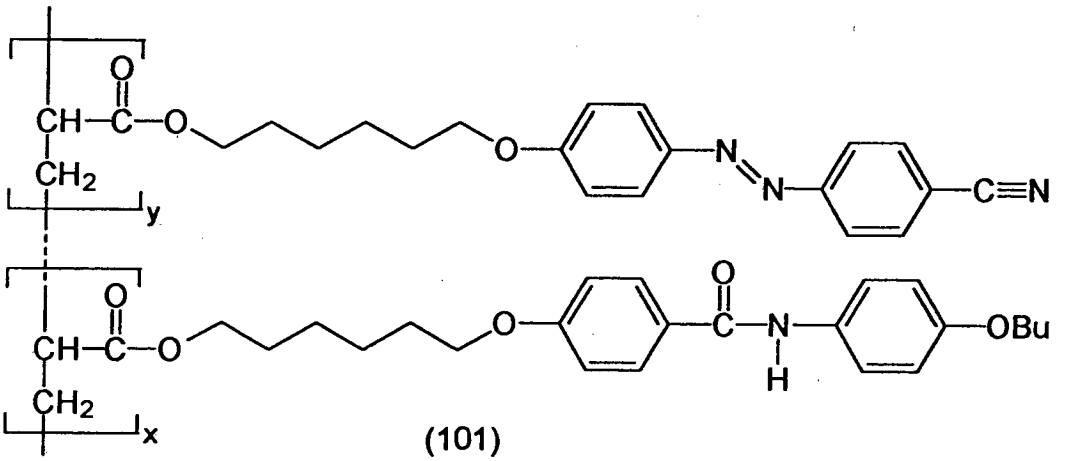
this device is due in some way to the isomerisation of the photochromic element between its ring-open (95) and ring-closed forms (96).

Photochromic compounds have been developed for application as photo-switchable receptors. Many structures have been suggested as photo-controlled receptors[124,125] whose binding of guest species could be controlled by irradiation. For example, certain thioindigo derivatives (Scheme 20) have been shown to exhibit marked differences in the ability of their *trans* form (97) and *cis* form (98) to bind potassium ions.[126] The *trans* form (97) has no acceptable site for guest ions. However, when the indigoid moiety is converted to the *cis* form (98), the two ether chains co-operatively bind the potassium ion. The ability of such species to capture and release metal ions has led to their application in the extraction of radioactive metal ions from waste produced by the nuclear power industry being suggested.[125]

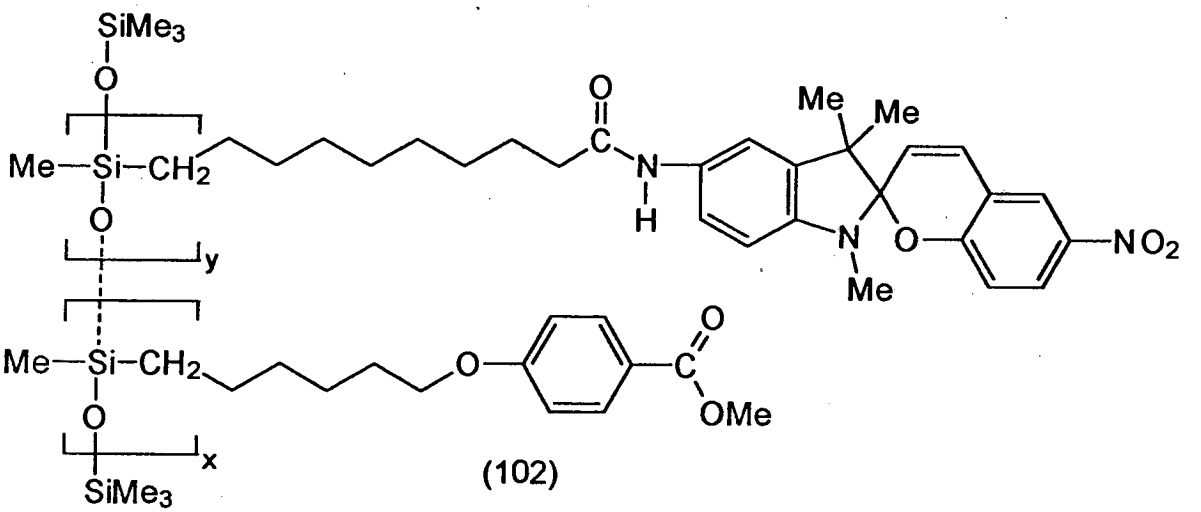
As early as 1956 it was suggested[127] that photochromic systems exhibiting two stable states could form the basis of a data storage system, (ie an optical, memory). Information could be 'written' with light of wavelength λ_1, 'read' with light of wavelength λ_2 and erased with light of wavelength λ_3. As photochromism is generally a molecular phenomenon it is a grainless system and hence high resolution (potentially down to the molecular level) is possible. Many publications and patents concerned with photochromic compounds have been motivated by the search for a suitable material for optical data storage.[128-129] An interesting example of this (Scheme 21) is the preparation of



(100)



(101)



(102)

Scheme 22

liquid crystal polymers (99) with fulgimide containing side chains.[131] The most rigorous demand on a potential optical recording material is the need for millions of 'read' / 'write' cycles without loss of reversibility, that is, no fatigue. This demand remains the biggest challenge to be overcome in the development of optical data storage.

Photochromic liquid crystal polymers have also been prepared for use in data display devices (Scheme 22). Liquid crystal polymers functionalised with spirooxazine[120] (100), azobenzene[132] (101) and spiropyran[133] (102) moieties have been prepared. The increase in understanding of the photochemical and thermal manipulation of spiropyran liquid crystal polymers (102) has led to the possibility of a display device which could display all three primary colours.[133] Compared with the fatigue resistance required in optical data storage, photochromic species incorporated into a display device would be required to change colour relatively few times. Use in imaging technologies may therefore be a more appropriate application for photochromic compounds.

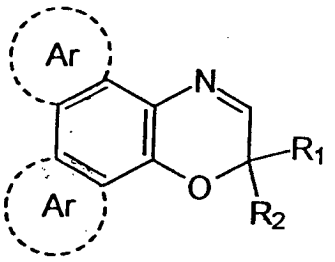
The use of photochromic compounds in eyeglasses is the most commercially significant application of photochromism.[70] The first photochromic spectacles to be marketed used glass lenses containing silver halide photochromics.[133] The growth in the use of lightweight plastic lenses (seventy percent of the market by 1989)[71] has led to the development of organic photochromic compounds suitable for incorporation into such lenses. Photochromic lenses must be near colourless in low lighting conditions becoming brown or grey in

sunlight. The rate of colour change should be readily perceptible for the wearer and roughly commensurate with the rate at which the retina adjusts to changes in illumination.[70] It has been estimated that the average spectacle wearer changes their glasses every two years.[70] The photochromic elements in spectacles should therefore be sufficiently fatigue resistant such that their behaviour is consistent over at least a two year period. An obvious candidate for inclusion into lenses are spiropyrans [see Page 11, Scheme 11; (50)] and 'non-spiro' 2*H*-benzopyrans [see Page 11, Scheme 12; (54)] as they generally absorb light across most of the visible spectrum (400-500 nm).[37] Though many pyran based photochromics are susceptible to fatigue which limits their useful lifetimes, some robust naphthopyrans (54, Ar=Ph) have been developed for use in lenses.[67] It has recently been reported that all plastic photochromic ophthalmic lenses currently being marketed contain at least one naphthopyran (54, Ar=Ph).[64] In contrast to many photochromic pyrans, spiro-2*H*-1,4-oxazines [see Page 11, Scheme 12; (56)] and structurally closely related condensed systems exhibit good fatigue lifetimes.[7] However, the merocyanine forms (57) can often only absorb in a limited region of the visible spectrum (550-630 nm). Due to their enhanced resistance to photodegradation, spirooxazines have been used in several plastic ophthalmic lenses marketed by the world's leading optical companies [eg Rodenstock, American Optical, Sola and Pittsburgh Plate Glass Industries (PPG)].[5] To produce a lens with the correct hue, and colouration and fade kinetics the use of mixtures of photochromic agents is required. Commercial photochromic lenses do slowly lose reversibility and therefore have a lifetime of around three years. The

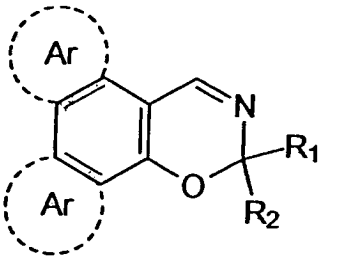
production of photochromic plastics for building or aircraft windows is desirable, though the three year lifetime of currently available materials limits this application.

CHAPTER 2

INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2*H*-1,4-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS

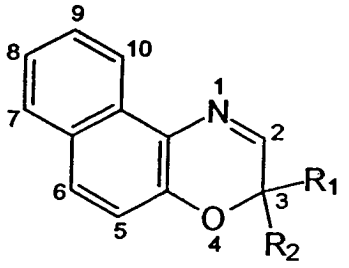


(103)



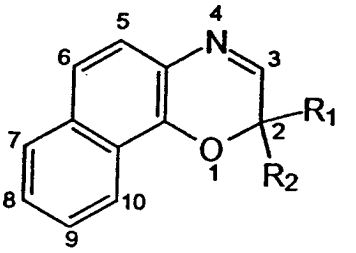
(104)

(Ar = Aromatic or heteroaromatic nucleus)



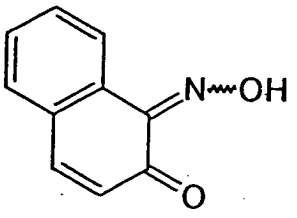
3*H*-Naphth[2,1-*b*]-1,4-oxazine

(105)



2*H*-Naphth[1,2-*b*]-1,4-oxazine

(106)



(107)

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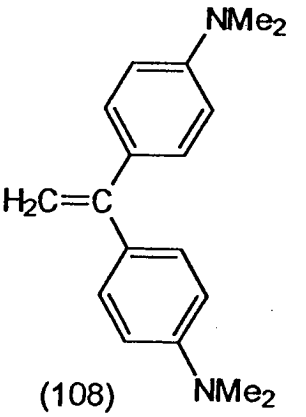
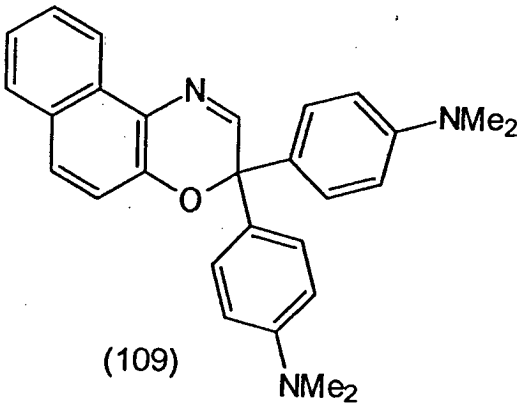


(108)

(i)



(109)

(i) AcOH, EtOH, reflux

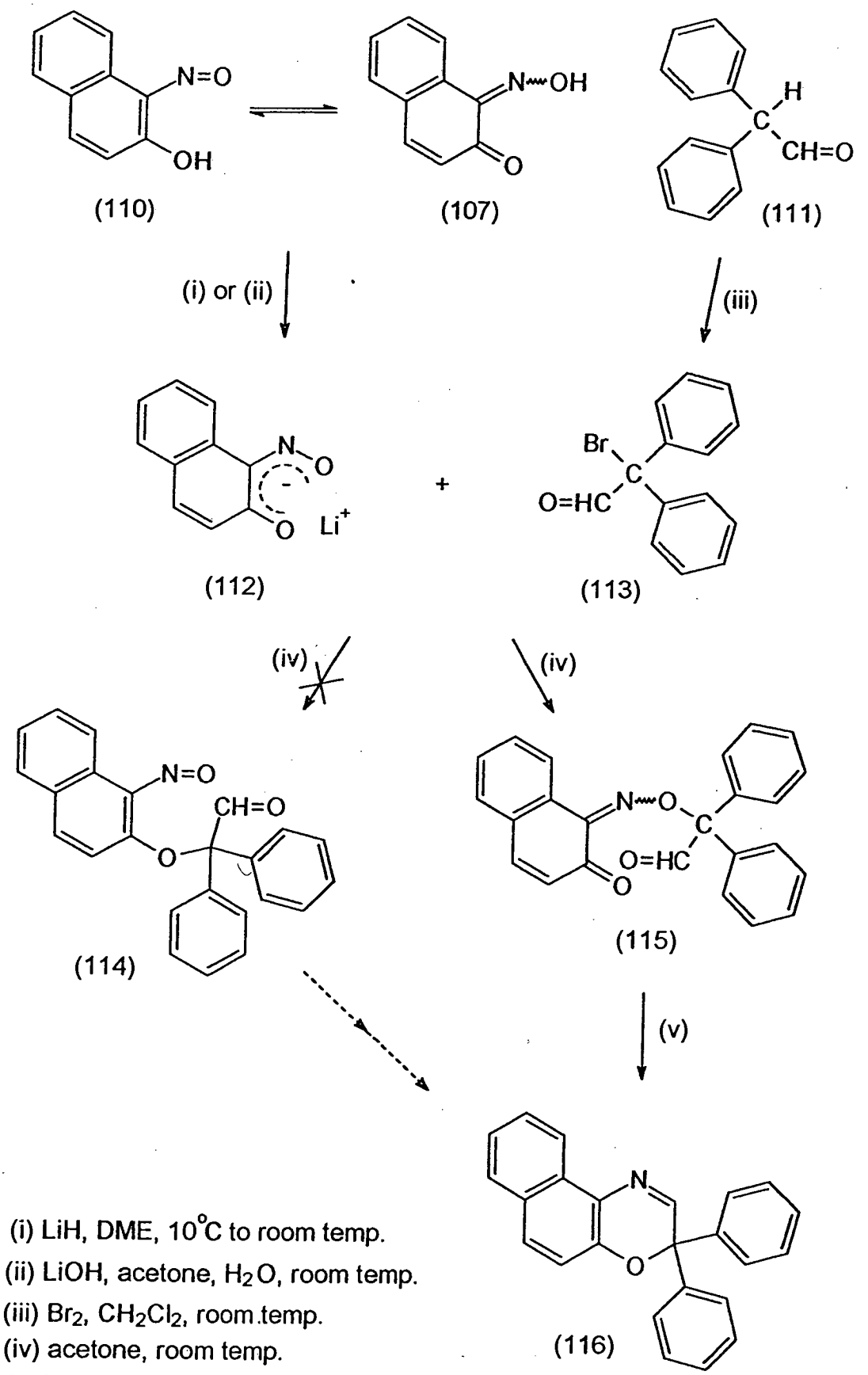
Scheme 23

2. INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2*H*-1,4-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS

2.1 Introduction

The foregoing chapter demonstrates some of the many applications of photochromic materials, the most commercially significant of which is in the production of ophthalmic lenses. There is an urgent need for new classes of photochromic molecules for this application which have good fatigue lifetimes, colour density and absorb over most of the visible spectrum. Certain compounds detailed in the previous chapter meet some of these requirements but are unsatisfactory in other respects. For example, fused 2,2-disubstituted 2*H*-benzopyrans [see Page 11, Scheme 12; (54)] and fused spiro-2*H*-benzopyrans [see Page 11, Scheme 12; (52)] absorb over much of the visible spectrum (400-550 nm). However, many such compounds are severely disadvantaged as practical photochromic agents due to poor fatigue resistance. In contrast, fused 2,2-spiro-2*H*-benz-1,4-oxazines [see Page 12, Scheme 12; (56)] exhibit high resistance to fatigue but absorb over a limited region of the visible spectrum (550-630 nm). It follows (Scheme 23), that simple (non-spiro) fused 2,2-disubstituted 2*H*-1,4-oxazines (103) and 2,2-disubstituted 2*H*-1,3-oxazines (104) (the synthesis of which is the subject of Chapter 3) might combine the spectral features of the fused 2,2-disubstituted 2*H*-benzopyrans (54) with the fatigue resistance of fused 2,2-spiro-2*H*-1,4-

oxazines (56) thus providing the required new types of fatigue-resistant and spectrally appropriate photochromic agents. To date, only one publication describing the synthesis of fused 2,2-disubstituted 2*H*-1,4-oxazine derivatives (103) has appeared in the primary literature. In a disappointingly vague paper, Paetzold[135] describes the synthesis of 3,3-di-(4-*N,N*-dimethylaminophenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (109) by the acid catalysed reaction of 1,2-naphthalenedione 1-oxime (107) with the alkene (108) but quotes no yields or quantities of reactants. Paetzold's work also forms the basis of a patent[131] describing the photochromism of the naphth-1,4-oxazine derivative (109). The work of Paetzold[135] was investigated during recent studies at Edinburgh[137] and while the di-(4-*N,N*-dimethylaminophenyl)naphthoxazine derivative (109) was obtained as described, the yield of the reaction was very poor (12%). Attempts[137] to optimise this synthesis made little progress and it can be concluded that the route described in Paetzold's work[135] is unlikely to be suitable for the production of (109) or any other commercially significant naphthoxazine derivatives on a large scale. Since the appearance of this work, two further patents[138,139] describing the synthesis of fused 2,2-disubstituted 2*H*-oxazine derivatives have been filed. In a patent by the Tokuyama Soda Company,[138] several 2,2-dialkyl-2*H*-benz-1,4-oxazines are reported. However, irradiation of the fused dialkylbenzoxazine derivatives described is not reported to give coloured species and the potential for their employment as practical photochromic agents is therefore limited. A variety of fused 2,2-diaryl-2*H*-benz-1,4-oxazine derivatives are claimed in a patent by Rodenstock.[139] Though the synthesis of several variously substituted fused

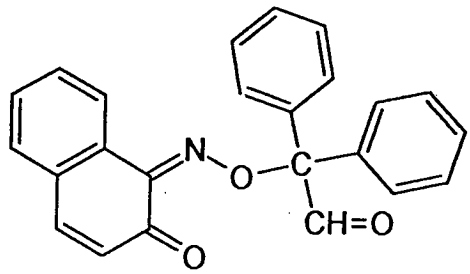


(i) LiH, DME, 10°C to room temp.
(ii) LiOH, acetone, H_2O, room temp.
(iii) Br_2, CH_2Cl_2, room.temp.
(iv) acetone, room temp.
(v) Ph_3P, THF or DME, reflux.

Scheme 24

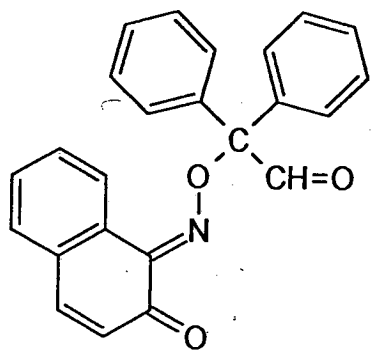
1,4-oxazine derivatives is claimed, very little data is offered regarding their characterisation and photochromism. In the light of the obvious deficiencies in the Rodenstock work and the limited scope of the two previously described patents, the preparation and photochromic characteristics of these compounds may be regarded as largely unexplored.

The lack of information on the potentially photochromic heterocyclic structures (103) and (104) provided the stimulus for recent studies at Edinburgh by Rowe[137] on the synthesis of disubstituted naphth-1,4-oxazine derivatives (105) and (106). Rowe[137] described the syntheses (Scheme 24) of the novel photochromic compound 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116) The strategy for the synthesis (Scheme 24) of the 3*H*-naphth[2,1-*b*]-1,4-oxazine derivative (116) involved the reaction of the lithium salt (112) of the tautomeric 1,2-naphthalenedione 1-oxime [(107) $\rightleftharpoons$ (110)] with 2-bromo-2,2-diphenylacetaldehyde (113). The two isomeric products of this condensation, isolated in good overall yield (79%), were initially thought to be two forms of the nitroso-aldehyde (114) and hence attempts were made to reduce the nitroso functionality to an amine. It was expected that following such a reduction, concurrent spontaneous cyclisation would occur affording the target naphthoxazine derivative (116). Thus, reduction of either form of the nitroso-aldehyde (114) with triphenylphosphine afforded the photochromic naphthoxazine derivative (116) in good yield (79%). Having successfully prepared the naphthoxazine derivative (116), the exact nature of the two nitroso-aldehyde species (114) was investigated. X-Ray diffraction analyses



(117)

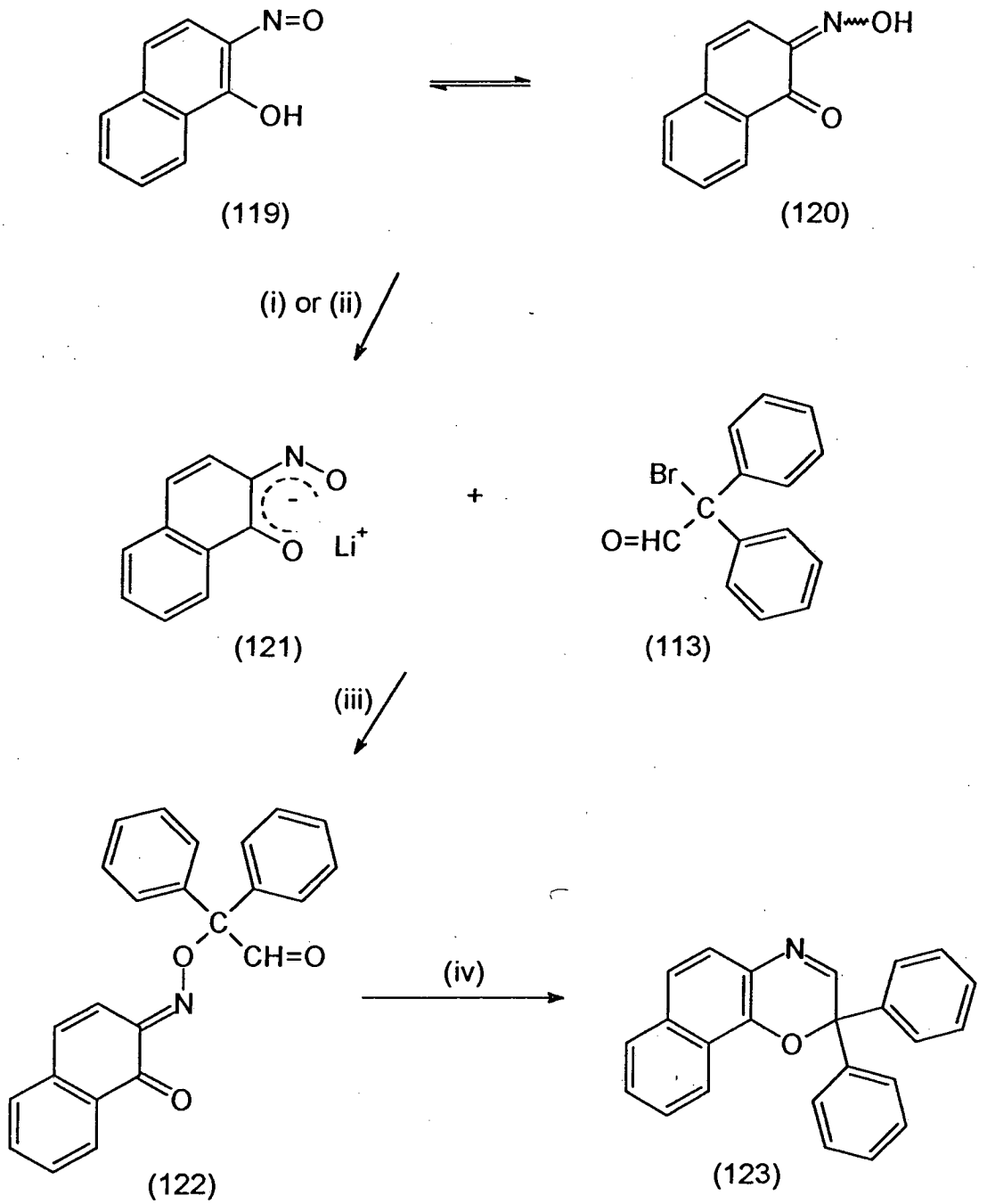
syn-1,2-Naphthalenedione 1-oxime diphenylformylmethyl ether



(118)

anti-1,2-Naphthalenedione 1-oxime diphenylformylmethyl ether

Scheme 25



(i) LiH, DME, 10°C to room temp.
(ii) LiOH, acetone, H_2O, room temp.
(iii) acetone, room temp.
(iv) Ph_3P, acetone, reflux.

Scheme 26

then revealed that the two products of the condensation of the lithium salt (112) and the bromo-aldehyde (113) were in fact *syn* and *anti* isomers of 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (115). The lithium salt (112), an ambident nucleophile, had reacted through the oximino oxygen and not as the nitrosonaphthoxide ion. The assignment (Scheme 25) of the two oxime ether structures as *syn* (117) and *anti* (118) is based on the orientation of the oximino functionality with respect to the quinone carbonyl. Having unequivocally established the structures of the isomers of the oxime ether (117) and (118), it is surprising that such species react (Scheme 24) with triphenylphosphine to give the naphthoxazine derivative (116). Little comment was made by Rowe[137] on the mechanism of this remarkable transformation which must involve a deep-seated rearrangement to account for the ultimate formation of the naphthoxazine derivative (116). Following the serendipitous discovery of this novel route to the naphthoxazine derivative (116), the analogous synthesis (Scheme 26) of 2,2-diphenyl-2*H*-naphth[1,2-*b*]-1,4-oxazine (123) was attempted.[137] Thus, the 1,2-naphthalenedione 2-oxime lithium salt (121) was prepared and reacted with 2-bromo-2,2-diphenylacetaldehyde (113) to give a product which was shown by X-ray diffraction analysis to be *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122). The oxime ether (122) was also found to react with triphenylphosphine giving the desired photochromic naphthoxazine derivative (123) in moderate yield (51%).

The studies described in this chapter are largely concerned with the optimisation and extension of the synthetic strategy described by Rowe[137] to give (Scheme 23) other potentially photochromic fused 2,2-disubstituted 2*H*-benz-1,4-oxazine derivatives (103). Synthesis of fused 2*H*-benz-1,4-oxazine derivatives functionalised at the 2-position with variously substituted aromatic moieties was considered desirable as was the synthesis of benz-1,4-oxazine derivatives fused to a variety of aromatic and heteroaromatic nuclei. Ultimately, it was hoped that the availability of new structurally diverse fused oxazine derivatives, by allowing the investigation of their photochemical properties, would provide a deeper insight into structure-photochromic activity relationships, thereby leading to the design of new practically useful photochromic materials.

2.2 Studies on the Synthesis of 3,3-Diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazine Derivatives

Initial studies under this heading centred on the optimisation of the synthesis (Scheme 24) of 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116) described by Rowe.[137] Thus, the key starting materials 2-bromo-2,2-diphenylacetaldehyde (113) and the lithium salt (112) of 1,2-naphthalenedione 1-oxime (107) were prepared. Commercially available diphenylacetaldehyde (111) was treated with bromine in dichloromethane at room temperature. Under these conditions a good yield (88%) of the bromo-aldehyde (113) was obtained. The

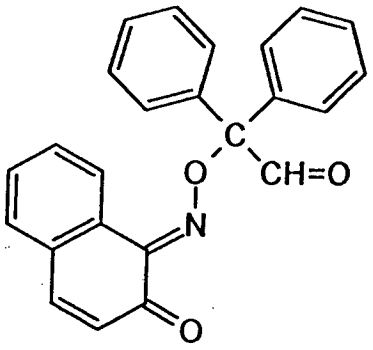
lithium salt (112) had previously been prepared[137] in excellent yield (95%) by the treatment of 1,2-naphthalenedione 1-oxime (107) with lithium hydride in anhydrous 1,2-dimethoxyethane. However, synthesis of the salt (112) by this method required that the 1,2-naphthalenedione 1-oxime (107) be purified by flash-chromatography prior to reaction and that anhydrous solvents be used for the reaction itself. Thus, a simpler method for the preparation of this key starting material was developed. Treatment of an acetone solution of crude, commercially available 1,2-naphthalenedione 1-oxime (107) with aqueous lithium hydroxide at room temperature gave a quantitative yield of the lithium salt (112) as a green solid with a metallic lustre. The lithium salt (112) and the bromo-aldehyde (113) condensed smoothly in acetone at room temperature to give (Scheme 25) a readily separable mixture of the orange *syn*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (117) in low yield (5%) and the yellow *anti* isomer (118) in moderate yield (57%). The reactivity (Scheme 24) of the bromo-aldehyde (113) towards 1,2-naphthalenedione 1-oxime (107) was next investigated in order to establish if it is necessary to prepare the lithium salt (112) prior to the condensation reaction. Treatment of 1,2-naphthalenedione 1-oxime (107) with bromodiphenylacetaldehyde (113) at room temperature in acetone gave none of the oxime ether (115). Instead, a high yield of the unreacted oxime (107) (69%) was obtained as was a gum containing unreacted bromo-aldehyde (113).

Anti-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [Scheme 25; (118)] reacted with triphenylphosphine in refluxing anhydrous 1,2-

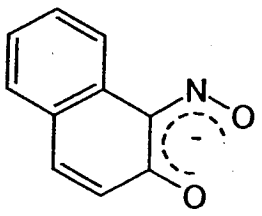
dimethoxyethane to give 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 24; (116)] in moderate yield (50%). In an effort to improve the yield of this transformation, the *anti* oxime ether (118) was reacted with triphenylphosphine in refluxing anhydrous tetrahydrofuran. Under these conditions the naphthoxazine derivative (116) was isolated in good yield (69%). In an alternative approach, the lithium salt of 1,2-naphthalenedione 1-oxime (112) was reacted with the bromodiphenylacetaldehyde (113) at room temperature in anhydrous 1,2-dimethoxyethane. The resulting crude reaction mixture was then treated with triphenylphosphine and heated under reflux. This 'one-pot' procedure afforded the naphthoxazine derivative (116) in moderate overall yield (41%).

As the mechanism of the conversion of the oxime ether (115) to the naphthoxazine derivative (116) was unclear, it was not known whether the transformation was specific to triphenylphosphine. Hence, use of another trivalent phosphorus reducing agent, triethyl phosphite was investigated. Reaction of the *anti* oxime ether (118) with triethyl phosphite in refluxing anhydrous 1,2-dimethoxyethane gave a complex gum from which only a small amount of benzophenone was isolated.

In an attempt to investigate the mechanism of the formation of the diphenylnaphthoxazine derivative (116) from the oxime ether (115), the thermolysis of the latter in the absence of triphenylphosphine was investigated. It was thought possible that the initial step in the formation of the



(118)



(124)

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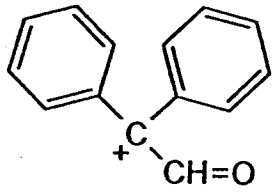
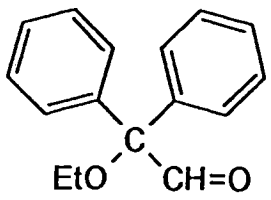


(125)

(i)



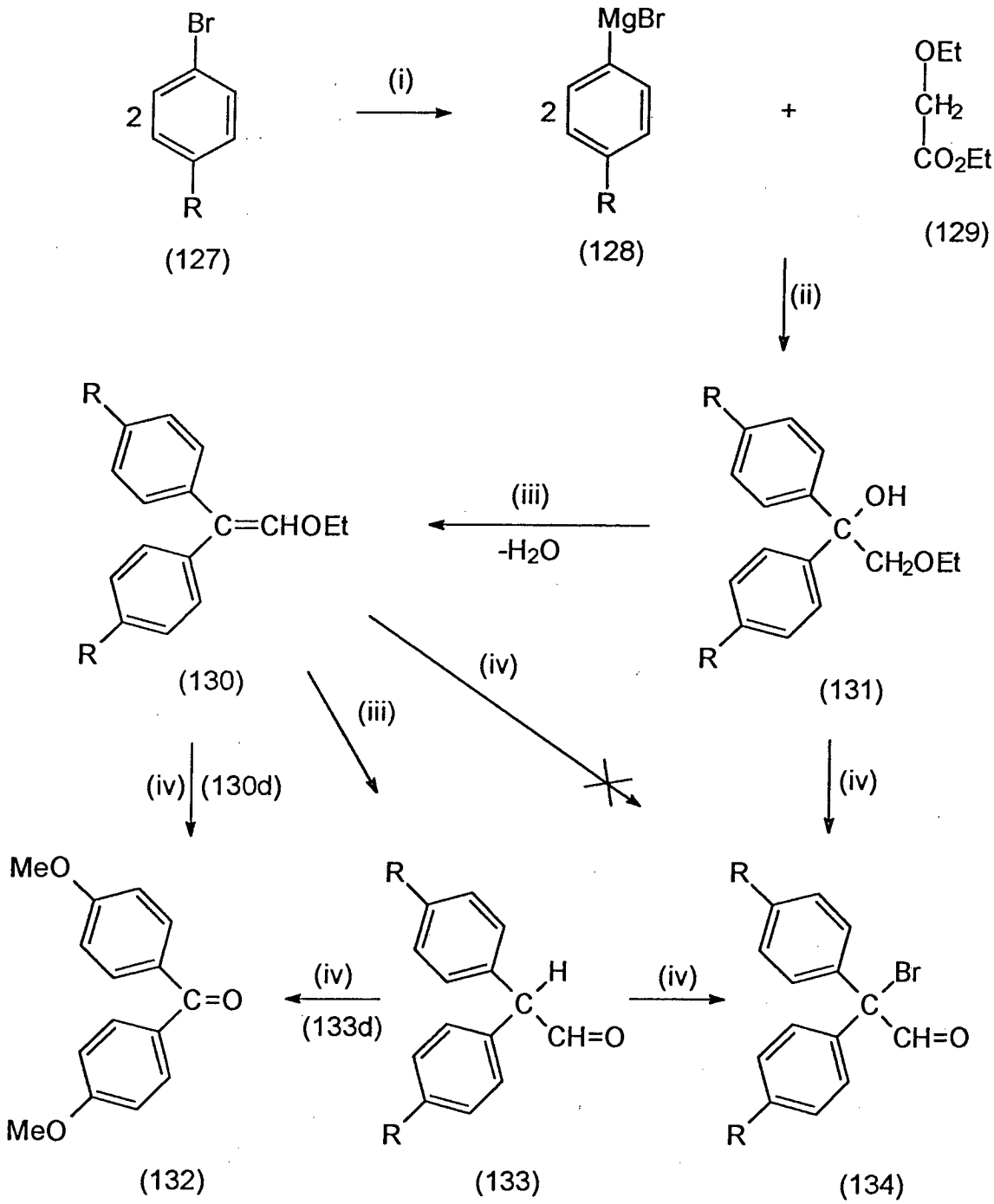
(126)

(i) EtOH, reflux.

Scheme 27

naphthoxazine derivative (116) involves the thermal rearrangement of the oxime ether (115) to the nitroso-aldehyde (114), followed by triphenylphosphine reduction of the nitroso functionality to an amine. Spontaneous cyclisation to the naphthoxazine derivative (116) would then be expected to occur. Thus, *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) was heated in anhydrous 1,2-dimethoxyethane in an attempt to isolate any nitroso-aldehyde (114) formed. However, flash-chromatography of the resulting mixture afforded unreacted *anti* oxime ether (118) and a solid shown by ^{13}C nmr to be a mixture of *syn* (117) and *anti* (118) isomers. It is unclear whether this mixture of isomers was initially isolated as such or if the pure *syn* isomer (117) was isolated and some equilibration occurred in solution prior to the nmr spectrum being recorded. As no evidence for the formation of the nitroso-aldehyde (114) was obtained from the thermolysis of the oxime ether (118) in 1,2-dimethoxyethane, the experiment was repeated in the higher boiling solvent 1,4-dioxane. However, thermolysis under these conditions gave only an intractable gum. Photolysis of a 1,4-dioxane solution of the *anti* isomer (118) also gave only a mixture of the *syn* (117) and *anti* (118) isomers.

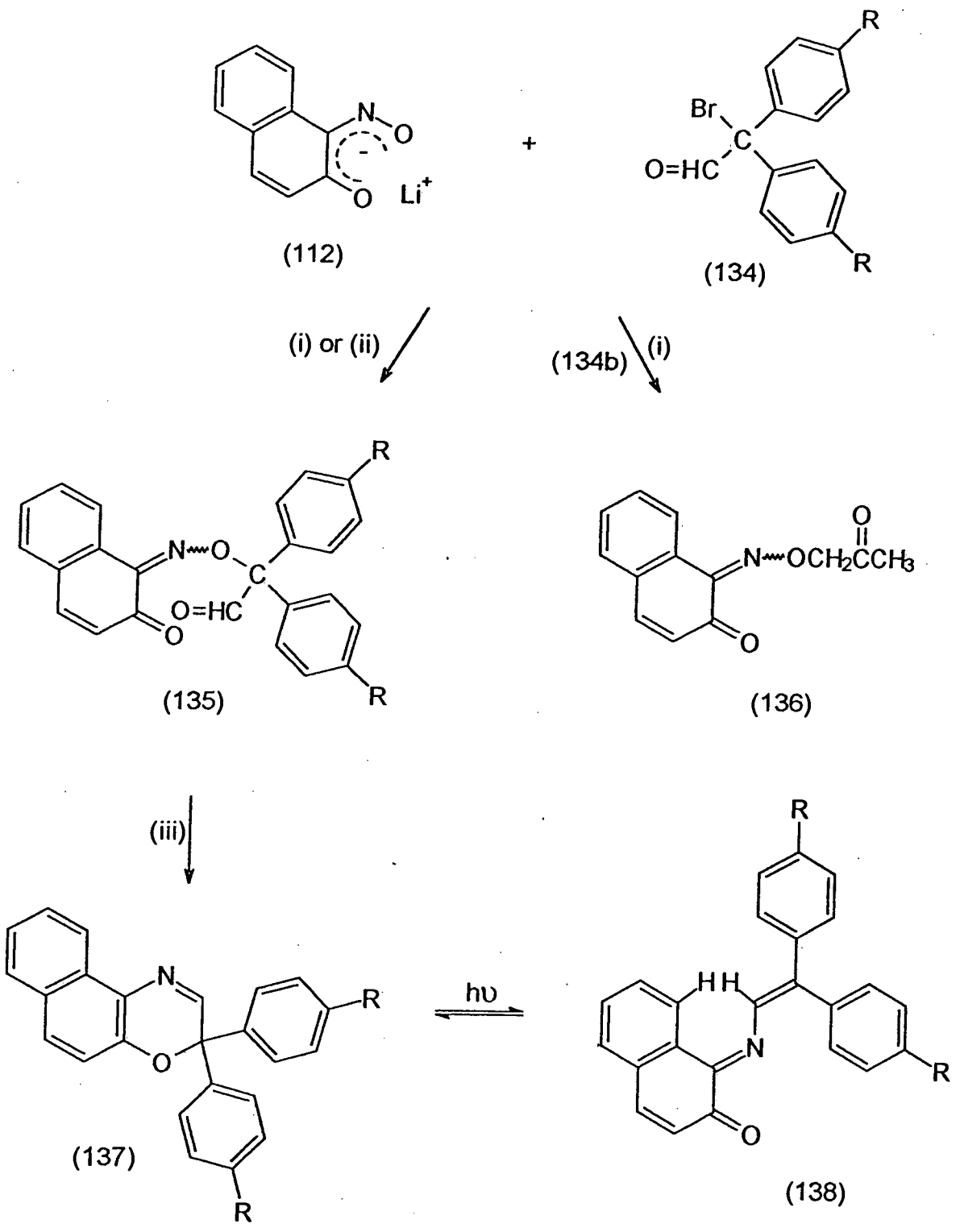
Having failed to isolate any identifiable product from the thermolysis of the *anti* oxime ether (118) other than the *syn* isomer (117), it was thought possible (Scheme 27) that the rearrangement taking place may involve short-lived charged intermediates such as (124) and (125). To investigate this, the *anti* oxime ether (118) was heated in anhydrous ethanol. It was hoped that any



(i) Mg, THF, (spontaneous reflux).
(ii) ether, reflux.
(iii) HCO_2H, H_2O, reflux.
(iv) Br_2, CH_2Cl_2, room temp.

R
a; Me
b; CF_3
c; NMe_2
d; OMe

Scheme 28



(i) acetone, room temp.
(ii) DME, room temp.
(iii) Ph_3P, DME, reflux.

R
a; Me
b; CF_3

Scheme 29

cationic species formed [eg (125)] would be trapped to give an ether [eg (126)]. In practice, thermolysis in ethanol gave only unreacted *anti* oxime ether (118) and a complex gum.

In parallel with the studies (Scheme 24) on the elucidation of the mechanism of the formation of the naphthoxazine derivative (116) from the oxime ether (115), studies were initiated on the application of this methodology to the synthesis of further 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazine derivatives. Initial studies centred on the synthesis (Scheme 28) of a range of bromodiarylacetaldehydes (134). Synthesis of novel bromo-aldehydes (134) was desired as their reaction (Scheme 29) with the 1,2-naphthalenedione 1-oxime lithium salt (112) was expected to give access to the oxime ether precursors (135) of novel naphthoxazine derivatives (137). The synthesis of novel diarylnaphthoxazine derivatives (137) whose aryl substituents are para substituted is worthy of investigation due to the observed effects[68] of such substitution on the corresponding naphthopyran (137; CH for N). Electron-donating para substituents generally cause a bathochromic shift (a shift to longer wavelength) in the visible spectrum of the ring-opened form (138; CH for N) while reversion to the parent pyran structure (137; CH for N) is accelerated. The effects of para substituents on the characteristics of the naphthoxazine derivatives (137) have never been explored and could ultimately prove valuable in the manipulation of these photochromic agents for commercial applications.

It was anticipated (Scheme 28) that 2,2-diarylacetaldehydes (133) would be generally accessible by a known[140] but little exploited route involving the reaction of arylmagnesium bromides (128) with commercially available ethyl 2-ethoxyacetate (129) and solvolysis of the resulting enol ethers (130) with refluxing formic acid. Thus, 4-bromotoluene (127a) was treated with magnesium in anhydrous tetrahydrofuran and the resulting Grignard reagent (128a) was heated with ethyl 2-ethoxyacetate (129) in anhydrous ether. The crude product of this reaction, isolated in quantitative yield, gave ^{1}H nmr and ir spectral data consistent with it being the ether-alcohol (131a) and not the enol ether (130a) which was described in the literature.[140] Thus the ir spectrum of this product shows an absorption at ν_{max} 3556 cm^{-1} and the ^{1}H nmr spectrum shows a broad singlet (δ_H 3.50-3.20) which is removed on addition of deuterium oxide. Both of these spectral properties are attributable to the hydroxyl functionality of (131a). Also present in the ^{1}H nmr spectrum is a two-proton singlet attributable to the methylene group and signals due to the ethyl group and the 4-methylphenyl moieties. As the tertiary alcohol (131a) would be expected to dehydrate readily [dehydration to give the enol ether (130a) being the first step in its conversion to the aldehyde (133a)], it is not surprising that the mass spectrum of the tertiary alcohol (131a) gives no parent ion but shows a peak corresponding to the enol ether (130a). Though attempts were made to purify the alcohol (131a) by distillation or flash-chromatography, decomposition resulted. Treatment of the tertiary alcohol (131a) with hot formic acid gave a colourless oil in good yield (67%) whose mass, ir and ^{1}H nmr spectral properties are fully in accord with its formulation as the aldehyde

(133a). Thus, the ir spectrum shows the expected aldehyde and carbonyl absorptions (ν_{max} 2721 and 1723 cm^{-1}) and the ^1H nmr spectrum shows, in addition to signals due to the methyl groups and aromatic protons, two one-proton doublets at δ_H 9.94 and 4.85 attributable to the aldehyde and methine protons.

In a parallel approach, the reaction of 4-methylphenylmagnesium bromide (128a) and ethyl 2-ethoxyacetate (129) was performed as previously described but no attempt was made to purify the apparently unstable tertiary alcohol (131a). Treatment of the crude alcohol with hot formic acid gave the aldehyde (133a), which was isolated in good yield (72%) following distillation.

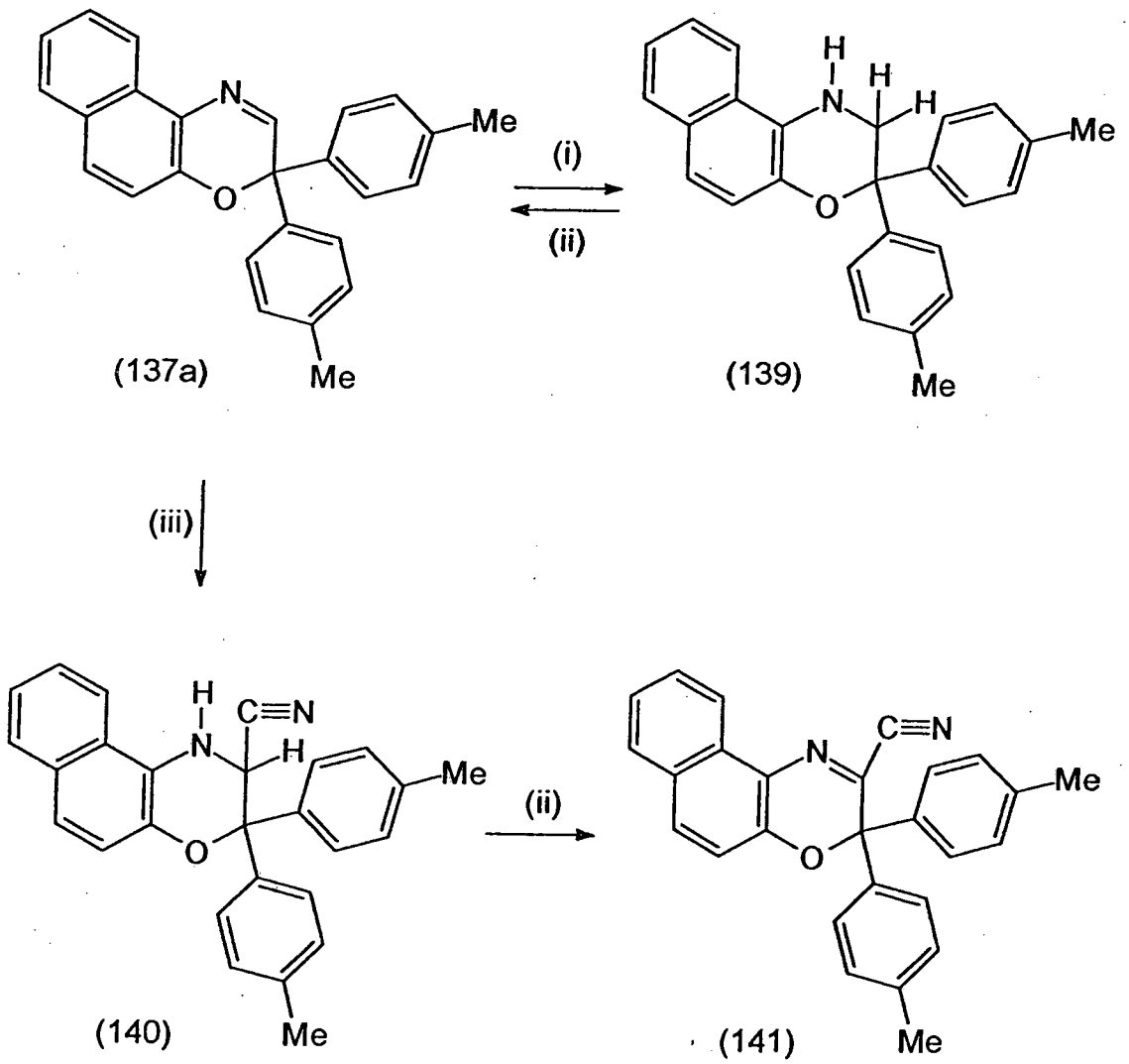
With the aldehyde (133a) to hand, its bromination was investigated. Using conditions identical to those used to brominate diphenylacetaldehyde [see Page 27, Scheme 24; (113)], the di-(4-methylphenyl)acetaldehyde (133a) was treated with bromine in anhydrous dichloromethane at room temperature. Reaction under these conditions afforded a quantitative yield of a red-brown oil whose ir and ^1H nmr spectral properties are consistent with its formulation as the bromo-aldehyde (134a). While the ir and ^1H nmr spectra of the 2,2-di-(4-methylphenyl)acetaldehyde (133a) and the brominated derivative (134a) are closely related, the signal due to the methine proton in the ^1H nmr spectrum of the former (δ_H 4.85) is, as expected, absent in the spectrum of the latter. An excellent yield (98%) of the bromo-aldehyde (134a) was also obtained through

bromination of 1,1-di-(4-methylphenyl)-2-ethoxy-1-hydroxyethane (131a) under the same conditions.

The bromo-aldehyde (134a) was found (Scheme 29) to condense smoothly with the 1,2-naphthalenedione 1-oxime lithium salt (112) in acetone at room temperature affording two crops of a product in moderate overall yield (53%). The first crop of the product, which was isolated as an orange solid in poor yield (14%), gave combustion analysis and ir spectral properties consistent with its formulation as the oxime ether (135a) but was shown by ^{1}H nmr spectroscopy to be a mixture of two isomers. This observation is directly comparable to the previously described 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [see Page 25, Scheme 25], which has been shown[132] to exist as *syn* (117) and *anti* (118) isomers. The second crop of product, isolated in moderate yield (39%) as a yellow solid, which also analysed correctly and gave an ir spectrum consistent with its formulation as the oxime ether (135a), was shown by ^{1}H nmr to be one of the compounds present in the first crop. Crystals of the two crops of product suitable for X-ray diffraction analysis were not obtained and hence to enable assignment of the structure of the two isomers of the di-(4-methylphenyl) oxime ether (135a), analogy is drawn from the spectroscopic properties of the two isomers of 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (Scheme 25) whose geometry was unequivocally established by X-ray diffraction.[137] The ^{1}H nmr spectra of the *syn* (117) and *anti* (118) isomers of the diphenyl oxime ether show signals due to their aldehydic protons at δ_H 9.96 and 10.05 respectively.

The aldehydic protons of the minor and major isomers of the di-(4-methylphenyl) oxime ether (135a) give signals in their ^{1}H nmr spectra at δ_H 9.91 and 10.00 respectively. The structure of the major isomer of 1,2-naphthalenedione 1-oxime di-(4-methylphenyl)formylmethyl ether (135a) is tentatively assigned as the *anti* isomer. The composition of the minor crop of product from this reaction is therefore assigned as a 3:5 mixture of *syn* and *anti* isomers. It is unclear whether the 3:5 mixture of isomers was initially obtained as such or whether the composition had changed in solution prior to the acquisition of its ^{1}H nmr spectrum.

Conversion of the di-(4-methylphenyl) oxime ether (135a) to the naphthoxazine derivative (137a) was next attempted. The *anti* isomer of the oxime ether (135a) was found to react with triphenylphosphine in refluxing anhydrous 1,2-dimethoxyethane to give a good yield (73%) of a tan solid whose analytical and spectroscopic properties are fully in accord with its formulation as 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a). Thus the ^{1}H nmr spectrum shows singlets attributable to the hydrogen atom of the imine moiety (δ_H 8.01) and methyl groups (δ_H 2.32) as well as a number of multiplets due to the aromatic protons. The naphthoxazine derivative (137a) was found to be photochromic under irradiation (254 nm) on a tlc plate. The ultraviolet/visible spectra and photochromic characteristics of the naphthoxazine derivatives prepared during these studies are discussed at the end of this chapter (see Section 2.7, Page 104).



(i) $NaBH_4$, H_2O, DME, room temp.

(ii) MnO_2, DME, room temp.

(iii) KCN, AcOH, 100°C.

Scheme 30

It is worthy of note at this juncture that the ring-opened form of the naphthoxazine derivative (137a) has more than one possible structure. Though the ring-opened form (138a) is shown with the imine functionality in an *anti* orientation with respect to the quinone carbonyl, a *syn* orientation is also possible. A noteworthy feature of the *anti* form (138a) is that the juxtaposition of the two highlighted hydrogen atoms is likely to destabilise the structure and cause rapid reversion to the bleached state (137a). Photolytic cleavage of the C-O bond of the naphthoxazine derivative (137a) could also result in a zwitterionic species in which the previously adjacent carbon and oxygen atoms are respectively positively and negatively charged. These speculative predictions of the structures of the open chain form (138a) can only be made at this stage by analogy with naphthopyrans[68] and spirooxazines[69,82] the coloured forms of which have been extensively studied.

To further support the structure of the previously undescribed naphthoxazine derivative (137a), investigations were made (Scheme 30) into its chemical behaviour as a cyclic imine and in particular towards hydride reduction. Thus, reaction of the naphthoxazine derivative (137a) with sodium borohydride in aqueous 1,2-dimethoxyethane at room temperature gave an excellent yield (95%) of a product which analysed correctly and gave mass, ir and ^{1}H nmr spectra which verify its formulation as the dihydronaphthoxazine derivative (139). Thus the ir spectrum shows the expected NH absorption band (ν_{max} 3408) and the ^{1}H nmr spectrum shows, in addition to signals due to the aromatic protons, a two-proton singlet at δ_H 3.95 due to the methylene group

and a broad one-proton signal (δ_H 3.70-3.20) which is removed on shaking with deuterium oxide and is therefore attributable to the amine hydrogen. Oxidation of the dihydronaphthoxazine derivative (139) using manganese dioxide in anhydrous 1,2-dimethoxyethane at room temperature regenerated the naphthoxazine derivative (137a) though in a disappointing yield (6%).

The reactivity of the naphthoxazine derivative (137a) towards nucleophilic addition of hydrogen cyanide across the imine bond was also investigated. Treatment of the naphthoxazine derivative (137a) with potassium cyanide in glacial acetic acid at 100°C gave an excellent yield (81%) of the dihydrocyanonaphthoxazine derivative (140). The combustion analysis and mass, ir and ^{1}H nmr spectra of the dihydrocyano compound (140) fully support its assigned structure. Thus the ir spectrum shows NH absorption bands at ν_{max} 3404 and 1630 cm^{-1} and a band due to the cyano moiety at ν_{max} 2238 cm^{-1}. The ^{1}H nmr spectrum shows a one-proton doublet due to the amino hydrogen (δ_H 4.67), which is removed on contact with deuterium oxide, and a one-proton multiplet (δ_H 5.36-5.34) which collapses to a singlet on addition of deuterium oxide. The latter, which is assignable to the methine proton shows a more complex splitting pattern than was expected. The reduced oxazine ring may exist in a number of conformations and the non-equivalence of the two methyl groups which are observed in the ^{1}H nmr spectrum at δ_H 2.33 and 2.20 suggests that over the nmr timescale, interconversion of these conformers is restricted. The reason for the complexity of the signal corresponding to the methine proton may also lie in these conformational effects. In further support

of this structure, the oxidation of the dihydrocyano compound (140) using manganese dioxide in 1,2-dimethoxyethane at room temperature was attempted. The product, which was isolated in quantitative yield, was identified as 2-cyano-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (141) by its mass and ir spectra.

Having prepared (Scheme 28) 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a) and successfully used it as a starting material in the synthesis of the corresponding naphthoxazine derivative, work was started on the analogous synthesis of (Scheme 29) 3,3-di-(4-trifluoromethylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137b). It was anticipated that the electron-withdrawing effect of the trifluoromethyl substituents in the latter might confer contrasting photochromic properties compared with the ditolyl derivative (137a). Thus, 4-bromobenzotrifluoride (127b) was treated with magnesium in anhydrous tetrahydrofuran and the resulting Grignard reagent (128b) was heated with ethyl 2-ethoxyacetate (129) in anhydrous ether. Distillation of the crude product of this reaction afforded a good yield (89%) of the ether-alcohol (131b) as a colourless oil whose combustion analysis and ir and ^{1}H nmr spectra support its assigned structure. As was observed in the mass spectrum of the di-(4-methylphenyl) alcohol (131a), the di-(4-trifluoromethylphenyl) alcohol (131b) gives no parent ion, giving instead a peak corresponding to the dehydrated product, the enol ether (130b).

With the alcohol (131b) to hand, its hydrolytic cleavage to the aldehyde (133b) was attempted. However, treatment of a refluxing 1,2-dimethoxyethane solution of the alcohol (131b) with aqueous hydrochloric acid gave only the unreacted starting material (131b). Repetition of this reaction using the higher boiling 1,4-dioxane as a solvent also gave the unreacted alcohol, in quantitative yield. However, conversion of the ether-alcohol (131b) to the aldehyde (133b) was achieved using hot aqueous formic acid. Reaction under these conditions gave the 2,2-di-(4-trifluoromethylphenyl)acetaldehyde (133b) in good yield (78%) as a red-brown oil which could not be purified without decomposition. In an alternative approach 4-trifluoromethylphenylmagnesium bromide (128b) was heated with ethyl 2-ethoxyacetate (129) in ether and the resulting crude alcohol (131b) was not purified but was treated with hot aqueous formic acid. Under these conditions the aldehyde (133b) was isolated in moderate overall yield (60%).

Bromination of the crude aldehyde (133b) was next attempted. Treatment of the aldehyde (133b) with bromine in anhydrous dichloromethane at room temperature gave good yield (82%) of the desired bromo compound (134b). Conversely, an attempt to brominate the ether-alcohol (131b) under the same conditions gave only unreacted starting material (83%). With the bromo-aldehyde (134b) now available, its condensation (Scheme 29) with 1,2-naphthalenedione 1-oxime lithium salt (112) was attempted at room temperature in acetone. Reaction under these conditions afforded none of the desired oxime ether (135b) giving instead unreacted bromo-aldehyde (134b)

(48%) and 1,2-naphthalenedione 1-oxime 2-oxopropyl ether (136) (15%). The oxopropyl oxime ether analysed correctly and gave ir and ^{1}H nmr spectra which support its assigned structure. Thus the ir spectrum shows two carbonyl absorption bands (ν_{max} 1728 and 1658 cm^{-1}) and the ^{1}H nmr spectrum shows a two-proton singlet at δ_H 5.11 and a three-proton singlet at δ_H 2.21 attributable to the oxopropyl group in addition to signals due to the protons of the naphthalene nucleus. While formation of the oxopropyl ether is surprising, it may be due to bromination of the acetone solvent by the bromo-aldehyde (134b) followed by reaction of the resulting bromoacetone with the lithium salt (112). This possibility is explored in an analogous reaction later in this chapter [see Page 91, Scheme 51; (228)]. Repetition of the reaction of the lithium salt (112) and the bromo-aldehyde (134b) at room temperature in anhydrous 1,2-dimethoxyethane gave only a complex gum from which no identifiable product could be isolated.

Attention was next turned to the synthesis (Scheme 28) of 2-bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (134c) and its use in a more efficient synthesis of 3,3-di-(4-*N,N*-dimethylaminophenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine than that known in the literature[135] [see Page 24; Scheme 23; (109)]. 4-*N,N*-Dimethylaminophenylmagnesium bromide (128c) was prepared by treatment of the bromo compound (127c) with magnesium in anhydrous tetrahydrofuran and was then heated with ethyl 2-ethoxyacetate (129) in anhydrous ether. Reaction under these conditions gave a cream solid in good yield (78%) whose combustion analysis and ir and ^{1}H nmr spectroscopic data are consistent with

its formulation as the ether-alcohol (131c). Treatment of the ether-alcohol (131c) with hot aqueous formic acid and trituration of the crude oily solid product afforded the aldehyde (133c) in excellent yield (86%) whose ir and ^{1}H nmr spectra support its assigned structure. Thus, the ir spectrum shows absorption bands at ν_{max} 2717 and 1714 cm^{-1} attributable to the aldehyde moiety and the ^{1}H nmr spectrum shows one-proton doublets at δ_H 9.77 and 4.62 attributable to the aldehyde and methine protons as well as signals due to the aromatic and *N*-methyl protons. However, a correct combustion analysis was not obtained for (133c) and its mass spectrum shows no parent ion giving instead a peak corresponding to the loss of a formyl group.

In a parallel experiment, 4-*N,N*-dimethylaminophenylmagnesium bromide (128c) was heated with ethyl 2-ethoxyacetate (129) in anhydrous ether then the resulting crude oily product was heated with aqueous formic acid. Basification of the resulting mixture gave the aldehyde (133c) as a green solid in poor yield (15%).

Bromination of 2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (133c) was attempted using bromine in anhydrous dichloromethane at room temperature. The green oily product so obtained was shown by its mass, ir and ^{1}H nmr spectra to contain the desired bromo compound (134c). However, attempts to purify the crude bromo-aldehyde (134c) resulted in its decomposition to a multicomponent oil. Bromination of 1,1-di-(4-*N,N*-dimethylaminophenyl)-2-ethoxy-1-hydroxyethane (131c) was also attempted but afforded a complex oil.

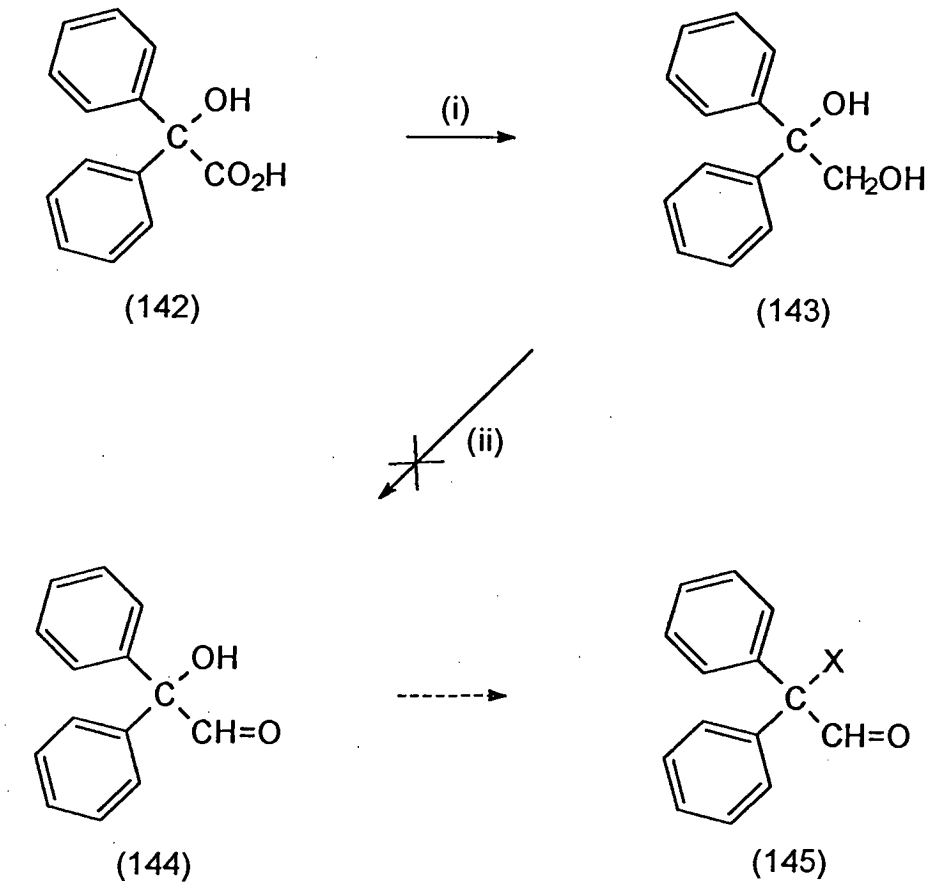
At this stage, no attempt was made to condense the bromo compound (134c) with a naphthalenedione oxime lithium salt [eg (112)]. Investigations into the synthesis of fused di-(4-*N,N*-dimethylaminophenyl)-2*H*-1,4-oxazine derivatives [see Page 89, Scheme 51; (231d)] using the bromo-aldehyde (134c) as a starting material are described later in this chapter.

Using the strategy that had proved successful in the synthesis (Schemes 28-29) of the di-(4-methylphenyl)naphthoxazine derivative (137a), work was also undertaken to synthesise 2-bromo-2,2-di-(4-methoxyphenyl)acetaldehyde (134d). 4-Methoxyphenylmagnesium bromide (128d) was prepared in anhydrous tetrahydrofuran then was treated with ethyl 2-ethoxyacetate (129) in anhydrous ether. In this case the Grignard reaction afforded a product in good yield (62%) which was shown by combustion analysis and mass, ir and ^{1}H nmr spectra to be the enol ether (130d) and not the ether-alcohol (131d). Thus the ^{1}H nmr spectrum shows a one-proton singlet (δ_H 6.45) as well as signals due to the ethyl and methoxy groups and the aromatic protons. In a similar experiment, 4-methoxyphenylmagnesium bromide (128d) was heated with ethyl 2-ethoxyacetate (129) but the resulting crude oil product was not purified to give the enol ether (130d). Instead, heating the crude product with aqueous hydrochloric acid gave a poor yield (13%) of 2,2-di-(4-methoxyphenyl)acetaldehyde (133d).

With the aldehyde (133d) to hand, attempts were made to achieve its bromination. Using the conditions employed for the bromination of previously

described diarylacetaldehydes, the dianisyl aldehyde (133d) was treated with bromine in anhydrous dichloromethane at room temperature. Under these conditions, the aldehyde (133d) decomposed giving a complex brown gum from which only a poor yield (26%) of 4,4'-dimethoxybenzophenone (132) was isolated. An alternative approach to the bromination of the dianisylacetaldehyde (133d) was next evaluated using the selective brominating agent tetrabutylammonium perbromide.[141] The perbromide was readily available[141] through treatment of tetrabutylammonium bromide with sodium bromate and hydrobromic acid in water at room temperature. Under these conditions tetrabutylammonium perbromide was isolated in moderate yield (62%). Treatment of 2,2-di-(4-methoxyphenyl)acetaldehyde (133d) with tetrabutylammonium perbromide in dichloromethane and methanol at room temperature gave only a complex gum whose ^{1}H nmr spectrum lacked any signal attributable to an aldehydic proton. Having failed to brominate the di-(4-methoxyphenyl)acetaldehyde (133d), work was undertaken to investigate the bromination of the di-(4-methoxyphenyl) enol ether (130d). Disappointingly, treatment of the enol ether (130d) with bromine in dichloromethane at room temperature also gave a complex gum from which only 4,4'-dimethoxybenzophenone (132) was isolated in poor yield (33%).

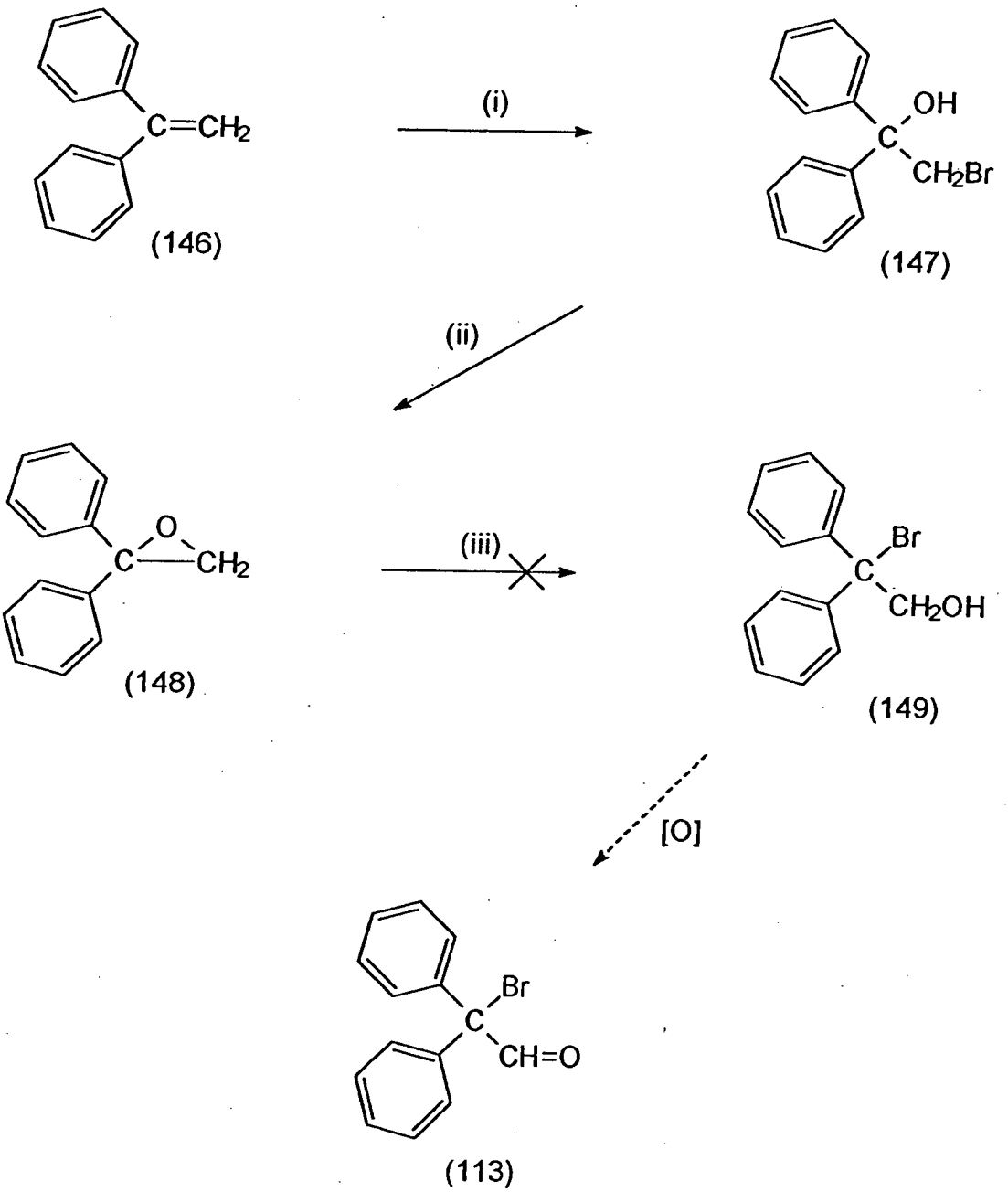
It was apparent that the bromination conditions described in the foregoing studies had limitations and were unsuitable for the synthesis of certain bromodiarylacetaldehydes which were required for the preparation of the corresponding diarylnaphthoxazine derivatives. Studies were therefore



(i) $LiAlH_4$, THF, reflux.

(ii) MnO_2, MeCN, room temp.

Scheme 31



(i) $MeC(=O)NHBr$, *t*-BuOH, H_2O, 0°C.

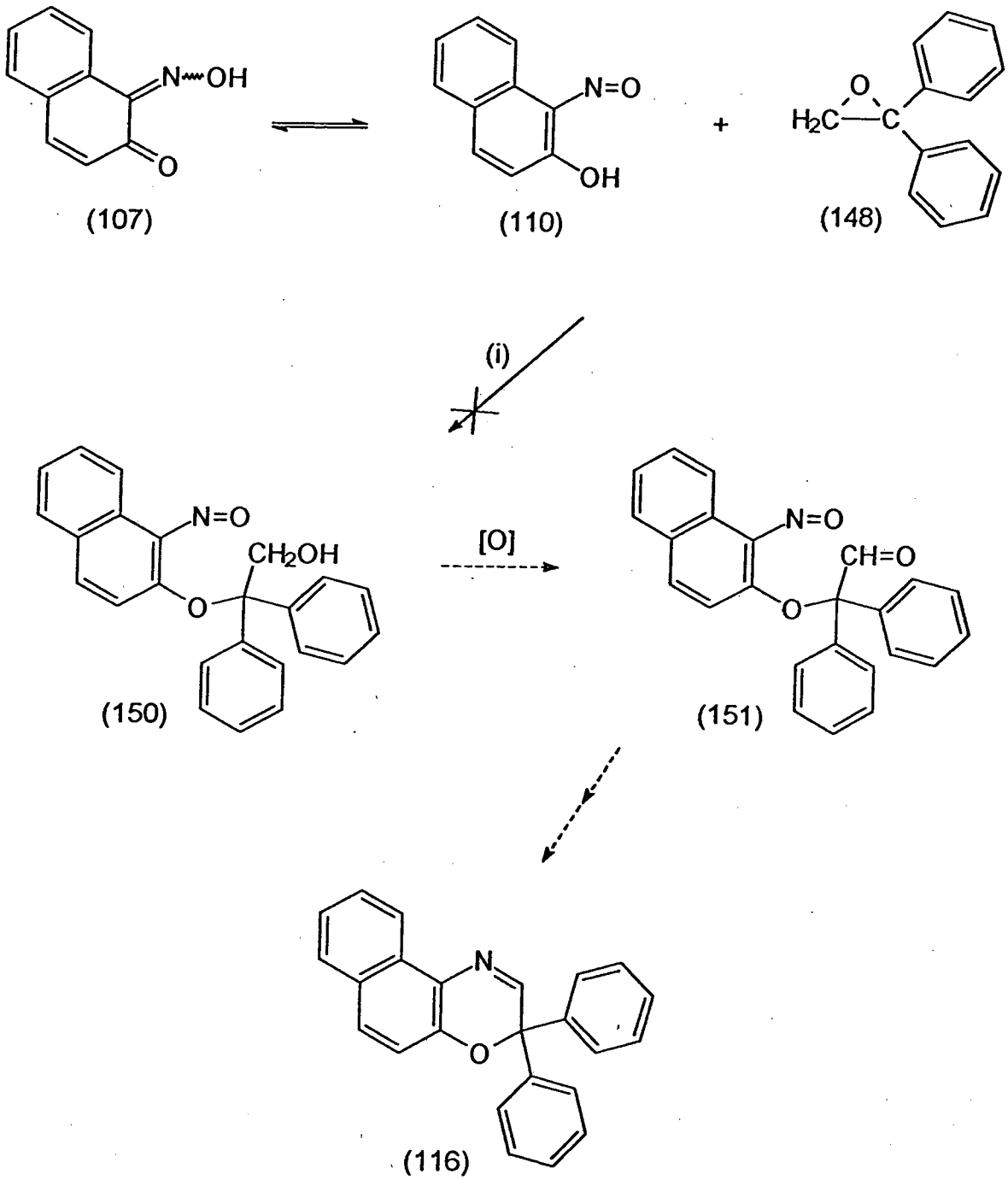
(ii) KOH, MeOH, 0°C.

(iii) HBr(g), ether, 0°C.

Scheme 32

initiated (Scheme 31) towards a general synthesis of α-functionalised diarylacetaldehydes other than bromo derivatives. It was hoped that the known[142] 1,2-diol (143), available from the reduction of benzylic acid (142), could be selectively oxidised to give the known[143] 2,2-diphenyl-2-hydroxyacetaldehyde (144). Conversion of the hydroxyl group of the latter into a good leaving group 'X' (eg triflate) would be expected to afford a species (145) which could react with a naphthalenedione oxime lithium salt (112) to give an oxime ether suitable for further elaboration to a photochromic naphthoxazine derivative. It was hoped that following success in this model synthesis of the parent diphenyl compound, the use of substituted benzylic acids as the source of the 1,2-diols would give access to α-functionalised diarylacetaldehydes whose bromo derivatives could not be synthesised using the previously described methodology. In practice, lithium aluminium hydride reduction[142] of benzylic acid (142) under reflux in tetrahydrofuran afforded the known[142] diol (143) though only in poor yield (29%). Attempted oxidation of the diol (143) with manganese dioxide in acetonitrile for 15 min at room temperature failed to give the desired hydroxyaldehyde (144) giving instead a mixture of products whose tlc indicated that it contained significant amounts of unreacted diol (143). Repetition of the attempted oxidation over 62 h gave only an intractable gum. Work towards the synthesis of 2,2-diphenyl-2-hydroxyacetaldehyde (144) was temporarily halted at this point.

Investigations on the development of an alternative general synthesis (Scheme 32) of 2-bromo-2,2-diarylacetaldehydes were continued in a further model

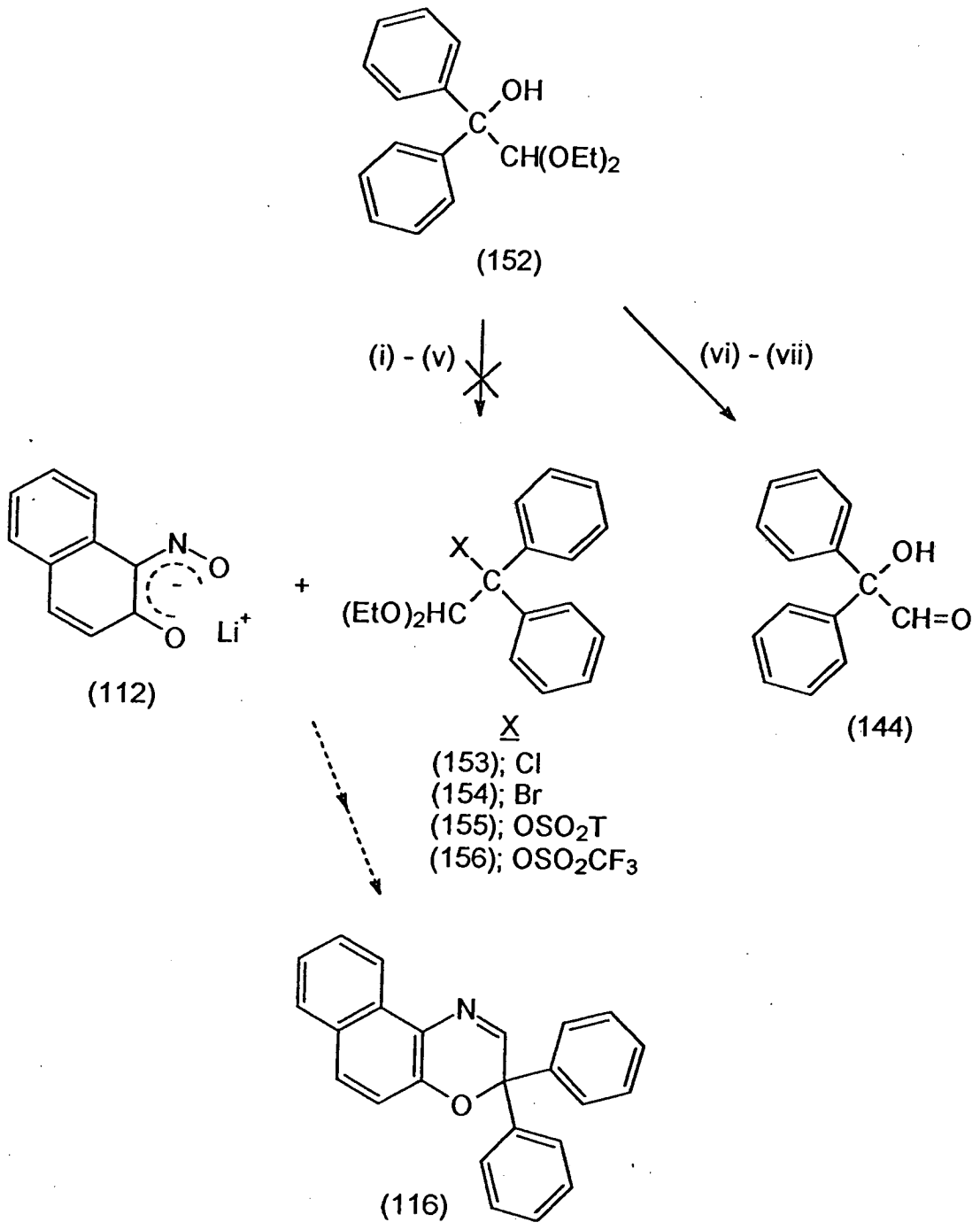


(i) ptsa, DME, room temp.

Scheme 33

study aimed at the preparation of the parent diphenyl compound (113). The proposed strategy involved the synthesis of the known[144,145] 1,1-diphenylethene epoxide (148) with a view to the investigation of its ring opening with hydrogen bromide. It was anticipated that the ring opening would afford the previously unreported bromohydrin (149) which could then be oxidised to the bromo-aldehyde (113). Thus, *N*-bromoacetamide was prepared[146] in poor yield (31%) by reaction of acetamide with bromine in the presence of potassium hydroxide at 0°C. Treatment of commercially available 1,1-diphenylethylene (146) with *N*-bromoacetamide in aqueous *t*-butanol gave the known[144] bromohydrin (147) in good yield (72%), then epoxide (148) was prepared[144] in excellent yield (88%) through treatment of the bromohydrin (147) with methanolic potassium hydroxide. Attention was next turned to the behaviour of the epoxide toward ring opening with hydrogen bromide. Unfortunately, saturation of an ether solution of the epoxide (148) with hydogen bromide afforded none of the desired bromohydrin (149) giving only an intractable gum.

In parallel with the foregoing studies a potential general route (Scheme 33) to naphth-1,4-oxazine derivatives [eg (116)] which did not rely on α-functionalised diarylacetaldehydes as starting materials was investigated. It was thought possible that acid catalysed reaction of 1,1-diphenylethene epoxide (148) with 1,2-naphthalenedione 1-oxime (107) may, if the latter were to react as its nitrosonaphthol tautomer (110), afford the ether (150) which would be suitable for further elaboration to the desired naphthoxazine derivative (116). Initial



(i) $SOCl_2$, CH_2Cl_2, room temp.
(ii) PBr_3, ether, -10°C to room temp.
(iii) PBr_3, DMF, 50°C.
(iv) TSO_2Cl, pyridine, room temp.
(v) $(F_3CSO_2)_2O$, Et_3N, CH_2Cl_2, -15°C.
(vi) CBr_4, Ph_3P, CH_2Cl_2, 0°C.
(vii) 2M HCl(aq), dioxane, reflux.

Scheme 34

attempts to investigate the ring opening behaviour of the epoxide (148) toward the tautomeric nitrosonaphthol [(107) ⇌ (110)] involved reaction in 1,2-dimethoxyethane at room temperature in the presence of toluene-4-sulphonic acid. Under these conditions, tlc indicated rapid consumption of the epoxide (148). Flash-chromatography of the multi-component product of this reaction afforded only a moderate recovery (43%) of 1,2-naphthalenedione 1-oxime (107) and none of the desired ether (150). In an alternative approach, the epoxide (148) was heated with the 1,2-naphthalenedione 1-oxime lithium salt [Scheme 29; (112)] in acetone. Under these conditions no reaction was observed and both starting materials were recovered unchanged in near quantitative yield.

Attention was once again turned to the synthesis (Scheme 34) of 2,2-diphenyl-2-hydroxyacetaldehyde (144). Having had some success in the synthesis (Scheme 28) of diarylacetaldehydes (133) through the reaction of aryl Grignard reagents (128) with ethyl 2-ethoxyacetate (129), a parallel strategy (Scheme 34) was postulated for the synthesis of diarylhydroxyacetaldehydes, which was initially applied to the synthesis of the parent diphenyl compound (144). It was hoped that reaction of phenylmagnesium bromide with the known[147] ethyl 2,2-diethoxyacetate [see Scheme 37; (162)] would afford the hydroxy-acetal (152) which can be considered as a protected form of the desired hydroxy-aldehyde (144). In practice, ethyl 2,2-diethoxyacetate was readily prepared[147] by heating commercially available dichloroacetic acid with sodium ethoxide followed by treatment with ethanolic hydrogen chloride and then neutralisation

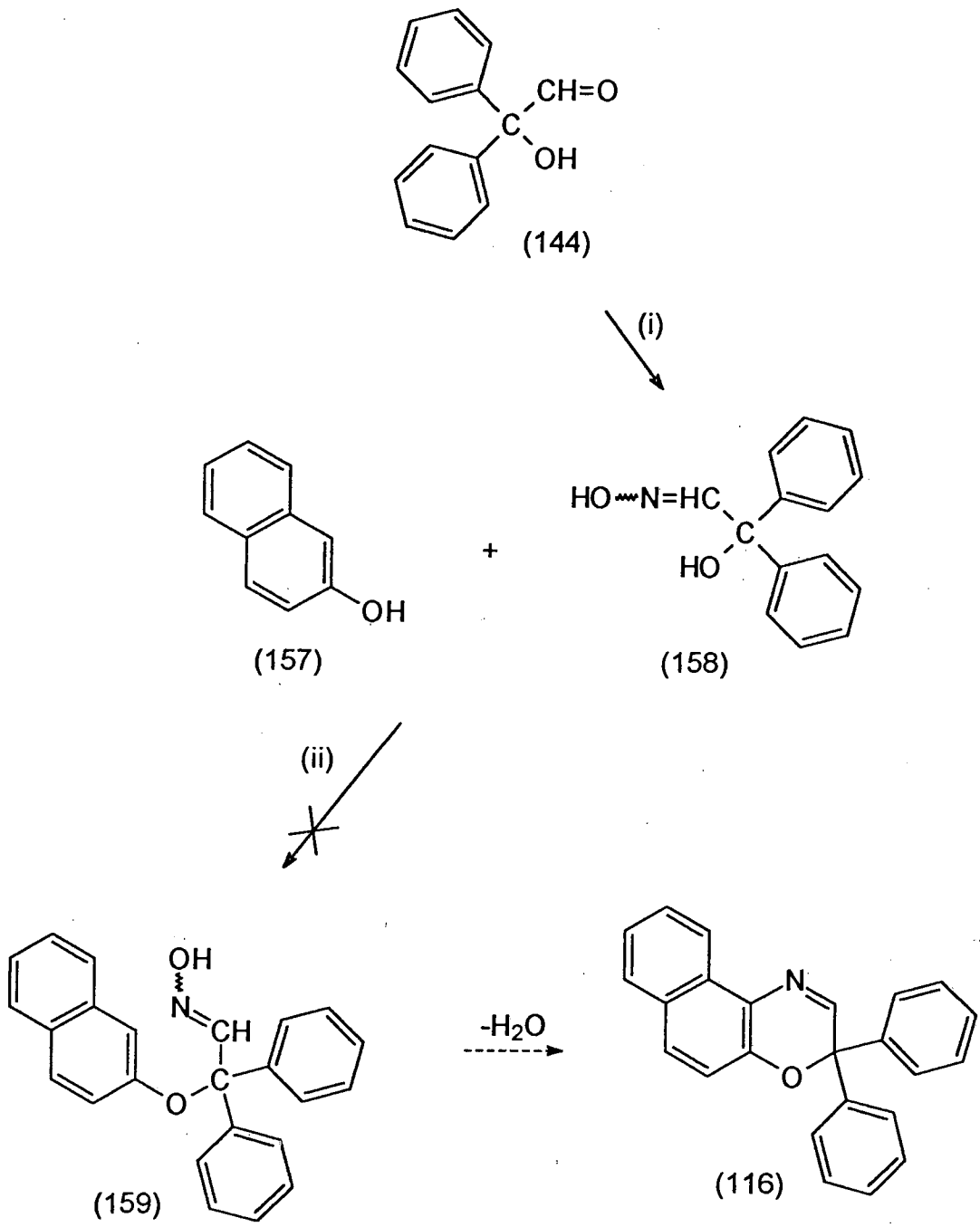
with further sodium ethoxide. Reaction under these conditions afforded a good yield (74%) of ethyl 2,2-diethoxyacetate whose structure was supported by its ir and ^{1}H nmr spectra. Reaction of ethyl 2,2-diethoxyacetate with phenylmagnesium bromide gave a good yield (65%) of the hydroxy-acetal (152) which analysed correctly and gave ir and ^{1}H nmr spectra consistent with the assigned structure. Thus, the ir spectrum shows the expected hydroxyl absorption band at ν_{max} 3559 cm^{-1} and the ^{1}H nmr spectrum shows signals due to the aromatic protons and the methine hydrogen (δ_H 4.92). Also present in the ^{1}H nmr spectrum are signals due to the ethyl groups in which the two methyl groups are coincident (δ_H 1.12) and the two-proton multiplets due to the methylene groups are non-equivalent (δ_H 3.82-3.67 and 3.39-3.24). This non-equivalence stems from the diastereotopic nature of the protons of the two methylene groups and is a phenomenon frequently observed in diethyl acetals.

Prior to attempts to convert the hydroxy-acetal (152) into the hydroxy-aldehyde (144) being made, work was started on the exchange of the hydroxyl functionality of (152) for a halogen or another good leaving group 'X'. Achievement of this would allow reaction with 1,2-naphthalenedione 1-oxime lithium salt (112) to be attempted. It was anticipated that an acetal oxime ether would result and that its acetal moiety could then be hydrolysed to give the oxime ether precursor to the desired naphthoxazine derivative (116). Thus, preparation of the chloro-acetal (153) was attempted by reaction of the hydroxy-acetal (152) with thionyl chloride in dichloromethane at room

temperature. Unfortunately, the resulting gum yielded no identifiable product. Bromination of the hydroxy-acetal (152) was attempted through treatment with phosphorus tribromide in ether at -10°C to room temperature but gave only a complex mixture. In a similar experiment the hydroxy-acetal (152) was heated to 50°C with phosphorus tribromide in dimethylformamide, but a complex gum was again obtained. A further attempt to brominate the hydroxy-acetal (152) using carbon tetrabromide and triphenylphosphine in dichloromethane at 0°C gave a moderate yield (56%) of an oil containing impure 2,2-diphenyl-2-hydroxyacetaldehyde (144).

Synthesis of the tosylate (155) and triflate (156) derivatives of the hydroxy-acetal (152) was also attempted. Thus, treatment of the hydroxy-acetal (152) with toluene-4-sulphonyl chloride in pyridine at room temperature gave only the unreacted hydroxy-acetal (152) (77%). Treatment of a dichloromethane solution of the hydroxy-acetal (152) with trifluoromethylsulphonic anhydride at -15°C also gave unreacted starting material (152) (52%) and a series of intractable gums.

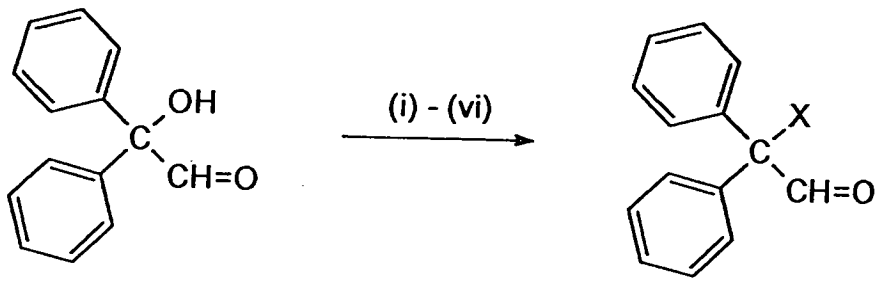
As work on the synthesis of an α-functionalised acetal suitable for use as a starting material in the synthesis of diarylnaphthoxazine derivatives [eg (116)] was proving fruitless, attention was turned to strategies involving use of the hydroxy-aldehyde (144). Treatment of the hydroxy-acetal (152) with dilute hydrochloric acid in refluxing 1,4-dioxane effected efficient hydrolysis giving an excellent yield (88%) of the hydroxy-aldehyde (144) whose combustion



(i) $NH_2OH.HCl$, Na_2CO_3, EtOH, room temp.

(ii) ptsa, toluene, reflux (Dean and Stark).

Scheme 35



(144)

X

(160); Cl

(113); Br

(161); OSO_2CF_3

(i) $SOCl_2$, CH_2Cl_2, room temp. to reflux.

(ii) HCl(g), $CaCl_2$, ether, 0°C to room temp.

(iii) HBr(g), $CaCl_2$, ether, 0°C to room temp.

(iv) PBr_3, ether, -10 to 0°C to room temp.

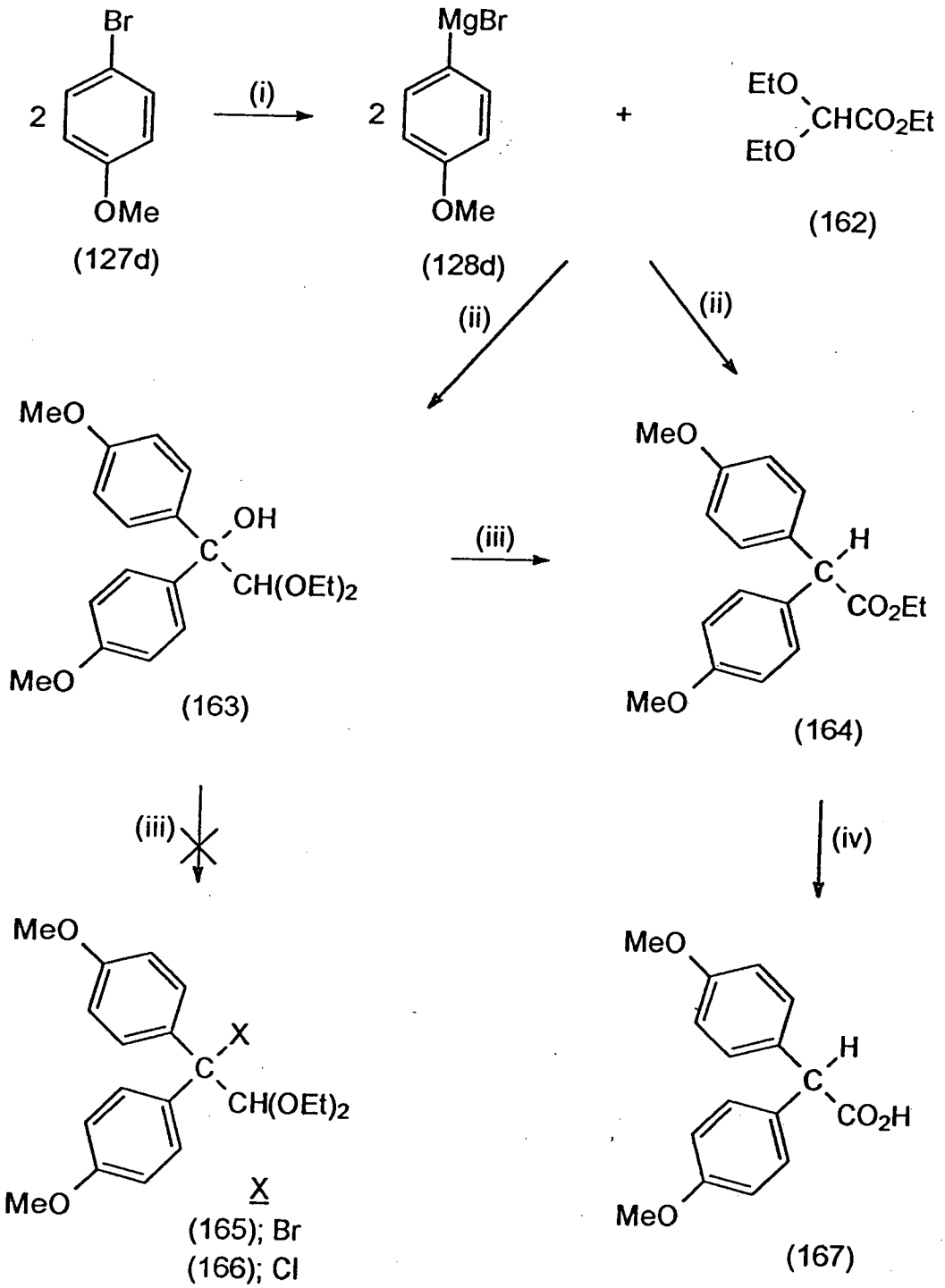
(v) CBr_4, Ph_3P, CH_2Cl_2, 0°C.

(vi) $(F_3CSO_2)_2O$, Et_3N, CH_2Cl_2, -15°C.

Scheme 36

analysis and ir and ^{1}H nmr spectra support its assigned structure. With the hydroxy-aldehyde (144) to hand, investigations were made (Scheme 35) on strategies for its use in the synthesis of naphthoxazine derivatives. It was anticipated that oximation of the hydroxy-aldehyde (144) would be straightforward and that the resulting hydroxy-acetaldoxime (158) would dehydratively couple with 2-naphthol (157) giving the ether (159). If obtained, the ether (159) could then be induced to dehydratively cyclise giving the desired naphthoxazine derivative (116). Thus, treatment of the hydroxy-aldehyde (144) with hydroxylamine hydrochloride in the presence of sodium carbonate at room temperature in anhydrous ethanol gave a good yield (67%) of 2,2-diphenyl-2-hydroxyacetaldoxime (158). Reaction of the hydroxy-acetaldoxime (158) with 2-naphthol (157) was attempted in the presence of toluene-4-sulphonic acid (ptsa) under reflux in toluene. Unfortunately, reaction under these conditions gave only intractable gums and a poor recovery (38%) of 2-naphthol (157).

Effort was then re-focussed on a strategy for conversion (Scheme 36) of 2,2-diphenyl-2-hydroxyacetaldehyde (144) to a species with a leaving group in the α-position [(160), (113) or (161)]. Treatment of the hydroxy-aldehyde (144) with thionyl chloride under reflux in dichloromethane gave only an intractable gum and none of the desired chloro compound (160). In an alternative approach the hydroxy-aldehyde (144) was treated with phosphorus tribromide in ether at 0°C to room temperature. Unfortunately, an intractable gum and not the desired bromo-aldehyde (113) was isolated from this reaction.



(i) Mg, THF, (spontaneous reflux).

(ii) ether, reflux.

(iii) HCl(g) or HBr(g), $CaCl_2$, ether, 0°C to room temp.

(iv) 2M NaOH(aq), reflux then conc. HCl, 0°C.

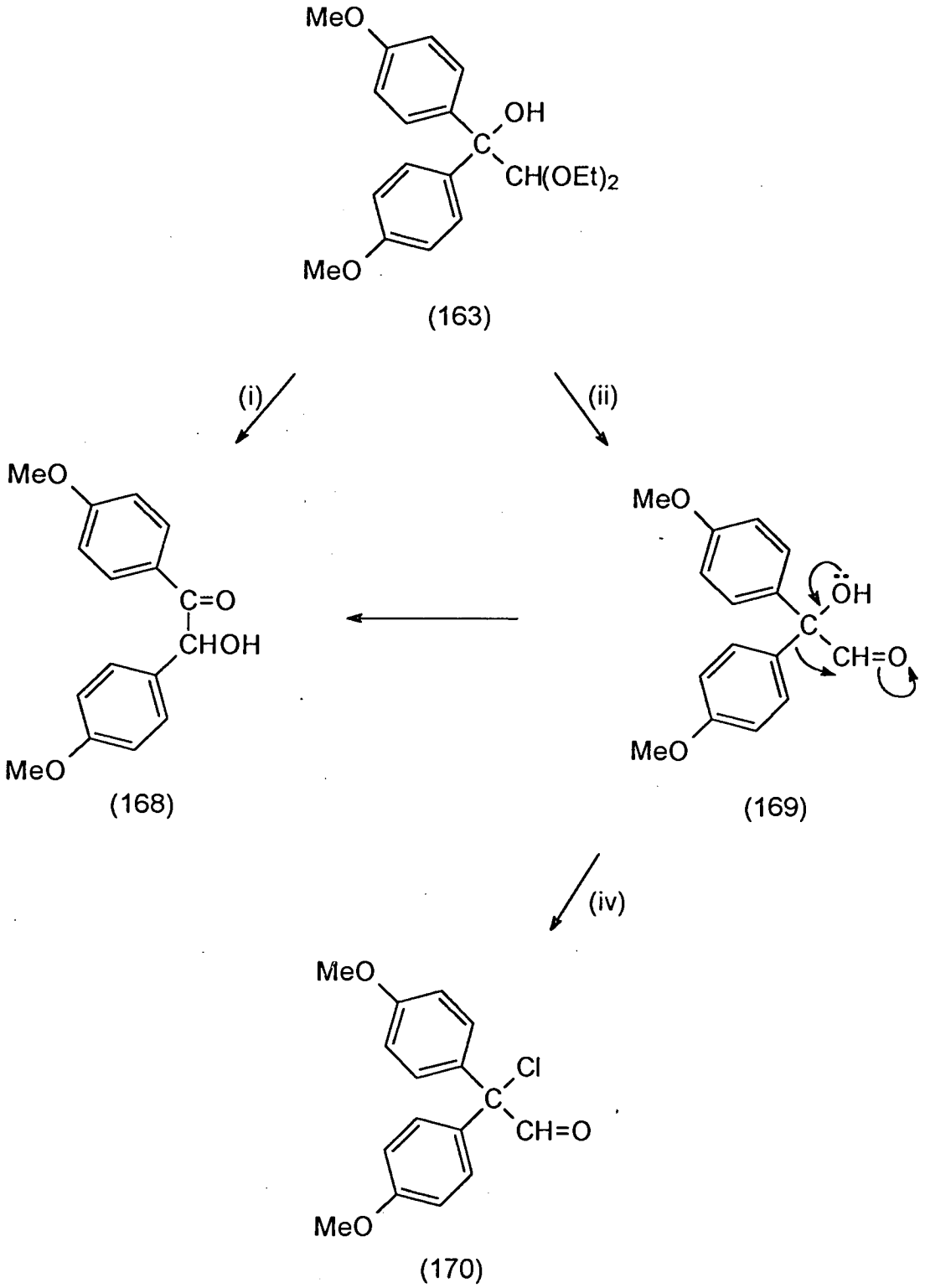
Scheme 37

Similarly, treatment of the hydroxy-aldehyde (144) with carbon tetrabromide and triphenylphosphine in dichloromethane at 0°C gave a complex gum. An intractable mixture also resulted from an attempt to prepare the triflate derivative (161) by treatment of the hydroxy-aldehyde (144) with trifluoromethanesulphonic anhydride in the presence of triethylamine in dichloromethane at -15°C. At this point a more detailed literature search revealed conditions[148] suitable for the chlorination of diaryl hydroxymethyl compounds which had not been attempted previously. Thus, the hydroxy-aldehyde (143) was treated with hydrogen chloride gas in the presence of calcium chloride in ether at 0°C to room temperature. While this reaction gave a complex oil, an analogous reaction using hydrogen bromide gas in the presence of calcium chloride in ether at 0°C to room temperature gave the bromo-aldehyde (113) in moderate yield (42%).

Having established alternative conditions for the preparation of α-bromo-aldehydes, work was undertaken to establish if these conditions would give access to certain bromo-aldehydes whose synthesis could not be achieved using bromine in dichloromethane [see Page 43, Scheme 28; (133)→(134)]. To this end, the synthesis of one of the previously inaccessible bromo-aldehydes, 2-bromo-2,2-di-(4-methoxyphenyl)acetaldehyde (134d) was attempted. Thus (Scheme 37), 4-methoxyphenylmagnesium bromide (128d) was heated with ethyl 2,2-diethoxyacetate (162) in ether. The mixture was then worked-up by treatment with water and dilute sulphuric acid and on quenching with water, a vigorous exotherm ensued. The product isolated from

the Grignard reaction was not the expected hydroxy-acetal. Mass, ir and ^1H nmr spectra revealed the product to be ethyl 2,2-di-(4-methoxyphenyl)acetate (164). The structure of the di-(4-methoxyphenyl) ester (164) was further evidenced by its hydrolysis to the corresponding carboxylic acid (167) with hot aqueous sodium hydroxide. The isolation of the ester (164) suggested that the desired hydroxy-acetal (163) had been formed but had then been converted to the ester (164) on work-up. Repetition of the Grignard reaction followed by cooling the reaction mixture prior to and during the work-up gave a good yield (72%) of the desired 2,2-diethoxy-1,1-di-(4-methoxyphenyl)-1-hydroxyethane (163).

Prior to attempts to hydrolyse the dianisyl hydroxy-acetal (163) being made, its halogenation was investigated as it was unclear whether halogenation followed by hydrolysis, or the same reactions in the reverse order, would most efficiently afford the desired bromo-aldehyde [Scheme 28; (134d)]. The hydroxy-acetal (163) was treated with hydrogen bromide gas in the presence of calcium chloride in ether at 0°C to room temperature. The oily product of this reaction was identified as impure ethyl 2,2-di-(4-methoxyphenyl)acetate (164). Elimination of the elements of ethanol from the hydroxy-acetal (163) under acidic conditions accounts for the formation of the ester (164). The ester (164) was also the product of an attempt to chlorinate the hydroxy-acetal (163). Treatment of an ether solution of the hydroxy-acetal (163) with hydrogen chloride gas in the presence of calcium chloride at 0°C to room temperature



(i) 2M HCl(aq), dioxane, reflux.

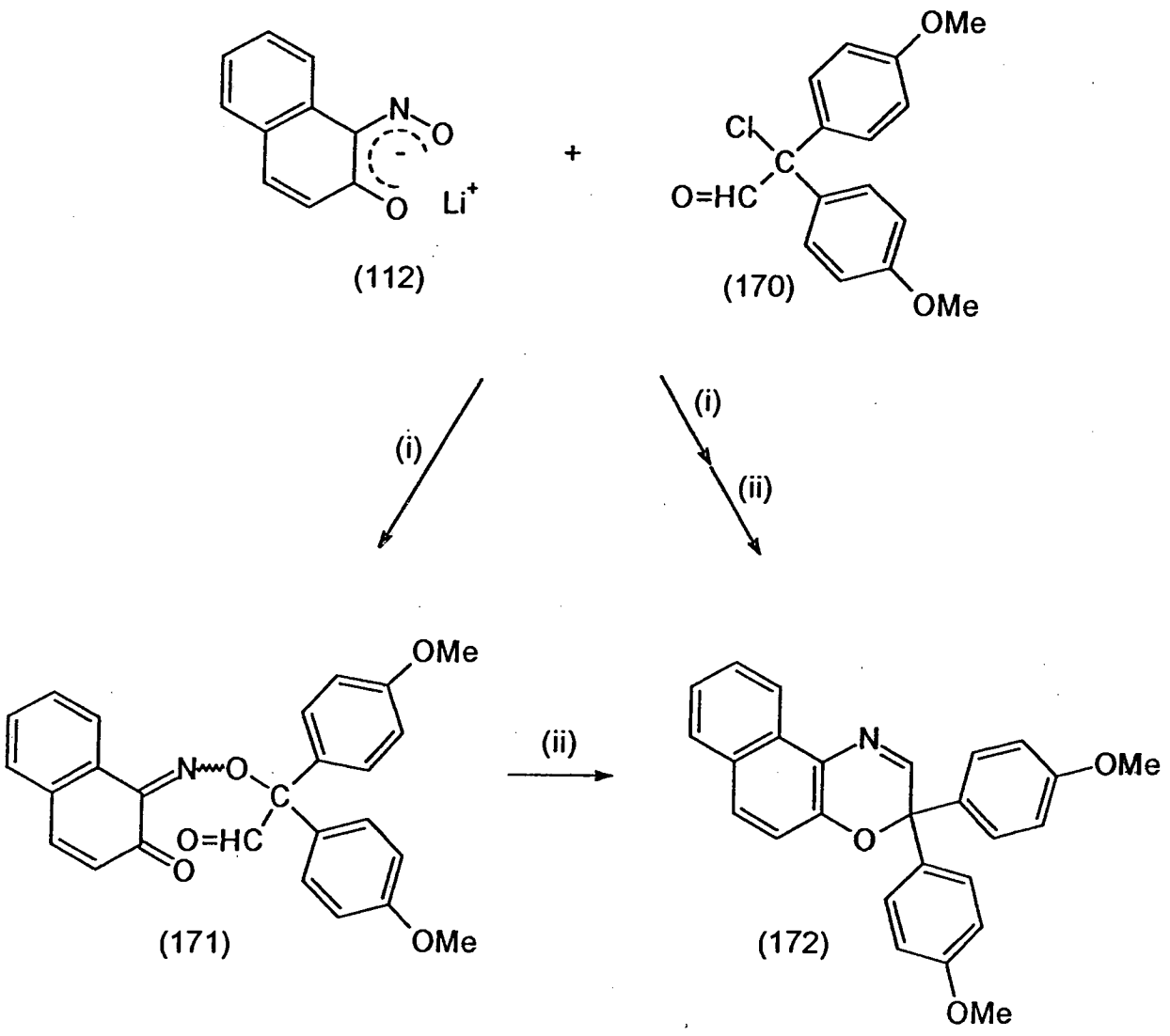
(ii) 2M HCl(aq), dioxane, room temp.

(iii) HCl(g), $CaCl_2$, ether, 0°C to room temp.

Scheme 38

gave none of the desired chloro-acetal (166) giving the ester (164) in high yield (87%).

The hydrolysis (Scheme 38) of the dianisyl hydroxy-acetal (163) to the hydroxy-aldehyde (169) was next attempted using the conditions under which the hydrolysis of the diphenyl hydroxy-acetal [see Page 48, Scheme 34; (152)] had been effected. However, treatment of the dianisyl hydroxy-acetal (163) with dilute aqueous hydrochloric acid in refluxing 1,4-dioxane afforded a moderate yield (64%) of 4,4'-dimethoxybenzoin (168) whose structure is supported by its combustion analysis and mass, ir and ^{1}H and ^{13}C nmr spectroscopic data. Thus the ir spectrum shows a hydroxyl absorption band at ν_{max} 3462 cm^{-1} and an absorption at ν_{max} 1663 cm^{-1} consistent with a carbonyl group conjugated to an aromatic nucleus. The ^{1}H nmr spectrum shows a one-proton doublet at δ_H 4.57 which is removed on shaking with deuterium oxide, attributable to the hydroxyl functionality and another one-proton doublet δ_H 5.84 due to the methine group which collapses to a singlet on contact with deuterium oxide. The formation of this product is probably due to the hydrolysis of the hydroxy-acetal (163) taking place as desired but followed by decomposition of the resulting hydroxy-aldehyde (169) via a pinacol-type rearrangement. The possible pinacol-type rearrangement [(169)→(168)] is illustrated by the curved arrows on (169). Repetition of the hydrolysis of the dianisyl hydroxy-acetal (163) with dilute hydrochloric acid in 1,4-dioxane at room temperature afforded an excellent yield (81%) of a colourless solid product whose combustion analysis and ir and ^{1}H nmr spectral properties support its formulation as the



(i) DME, room temp.

(ii) Ph_3P, DME, reflux.

Scheme 39

desired 2,2-di-(4-methoxyphenyl)-2-hydroxyacetaldehyde (169). Thus the ir spectrum shows the expected hydroxyl and carbonyl absorption bands (ν_{max} 3427 and 1722 cm^{-1}) and the ^1H nmr spectrum shows a one-proton doublet (δ_H 4.28) which is removed on contact with deuterium oxide and is attributable to the hydroxyl group and a one-proton doublet due to the aldehyde group (δ_H 9.86) which collapses to a singlet on shaking with deuterium oxide. The mass spectrum of the hydroxy-aldehyde (169) shows no molecular ion but gives a signal corresponding to the loss of the formyl group.

While chlorination of the dianisyl hydroxy-acetal [see Page 51, Scheme 37; (163)→(166)] was unsuccessful, chlorination (Scheme 38) of the hydroxy-aldehyde (169) proceeded smoothly. Treatment of the hydroxy-aldehyde (169) with hydrogen chloride gas in the presence of calcium chloride at 0°C to room temperature in ether gave an excellent yield (96%) of an oil in whose mass, ir and ^1H nmr spectra are consistent with it being the chloro-aldehyde (170). Due to the success of this chlorination, no attempt to brominate the hydroxy-aldehyde (169) was made.

Having isolated the chloro-aldehyde (170), its use (Scheme 39) as a starting material in the synthesis of 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172) was investigated. The chloro-aldehyde (170) was condensed with the 1,2-naphthalenedione 1-oxime lithium salt (112) at room temperature in 1,2-dimethoxyethane. Reaction under these conditions gave unreacted lithium salt (25%) and two crops of product. The first crop, an orange-brown

solid isolated in a poor yield (12%), gave combustion analysis and ir and ^{1}H nmr spectroscopic data consistent with it being 1,2-naphthalenedione 1-oxime di-(4-methoxyphenyl)formylmethyl ether (171) and a mass spectrum containing a peak corresponding to loss of a formyl group. The ir spectrum of the oxime ether (171) shows two carbonyl absorption bands (ν_{max} 1726 and 1651 cm^{-1}), while the ^{1}H nmr spectrum indicates the presence of two isomers in an 8:1 ratio giving two signals due to aldehydic protons at δ_H 9.96 and 9.87 as well as the expected aromatic and methoxy resonances. That the oxime ether (171) exists as two isomers is no surprise as both the previously synthesised diphenyl oxime ether [see Page 26, Scheme 25; (117) and (118)] and the di-(4-methylphenyl) oxime ether [see Page 34, Scheme 29; (135a)] were shown to exist as *syn* and *anti* isomers, the former case having been proved by X-ray diffraction studies.[137] The second crop of product, isolated in moderate yield (35%) as a yellow solid had analytical and spectroscopic properties consistent with it being a single isomer of the oxime ether (171). The two carbonyl groups give absorption bands in the ir spectrum at ν_{max} 1736 and 1666 cm^{-1} and the ^{1}H nmr spectrum shows a one-proton singlet at δ_H 9.96 attributable to an aldehyde group as well as signals attributable to the aromatic protons and methoxy groups. With the aim of assigning the geometry of the two isomers of the oxime ether (171), attempts were made to obtain crystals suitable for X-ray diffraction analysis. Analysis of a crystal of the crop of product containing a single isomer, reveals (Figure 3, Page 55) the oximino functionality to have an *anti* orientation with respect to the quinone oxygen. The bond lengths and

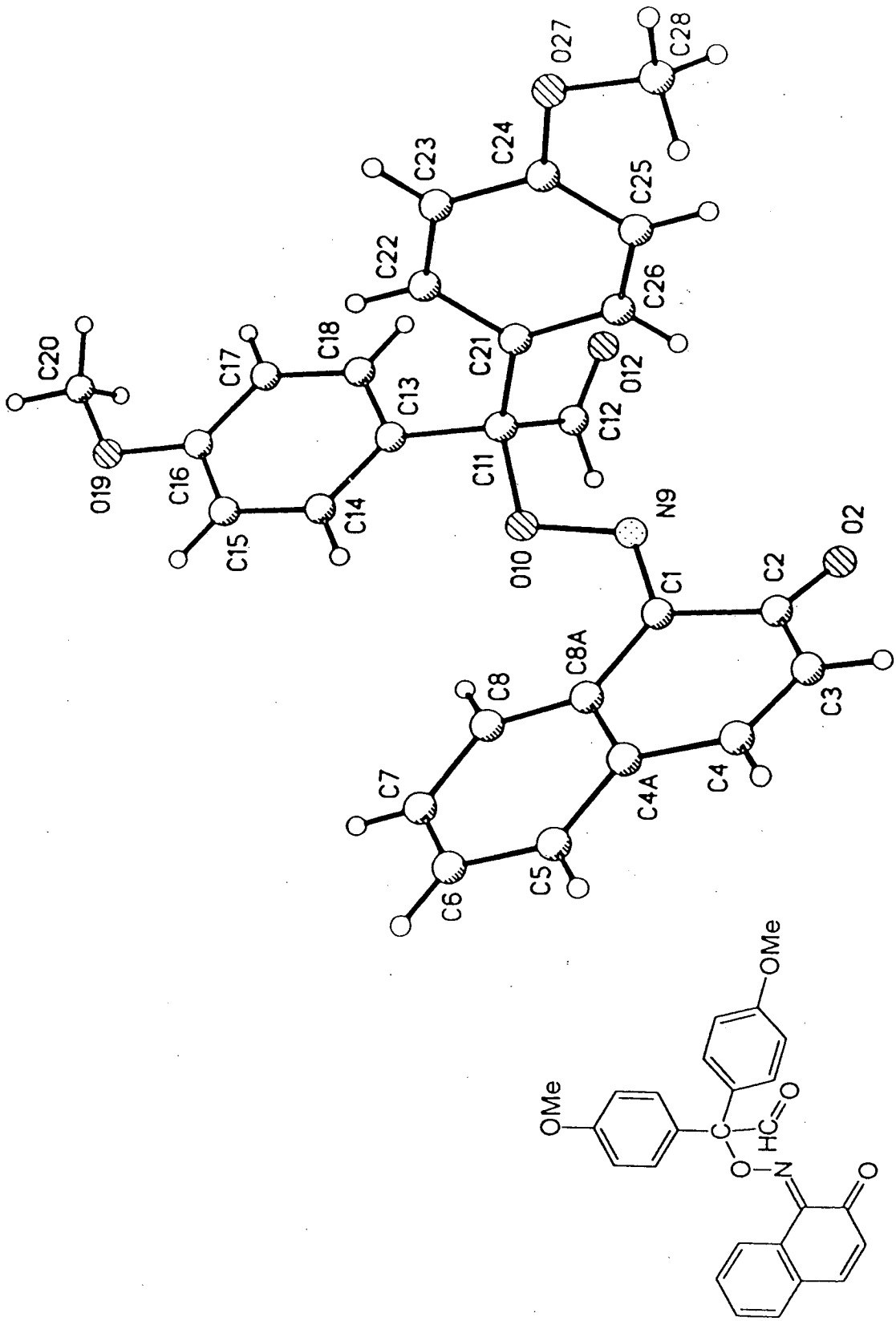
X-Ray Diffraction Data for *Anti*-1,2-naphthalenedione 1-Oxime Di-4-(methoxyphenyl)formylmethyl Ether (171)

Table 1: Bond Lengths (Angstroms) with Standard Deviations

C(1)-N(9)	1.292(2)	0(12)-C(12)	1.197(2)
C(1)-C(8A)	1.464(3)	C(13)-C(14)	1.383(3)
C(I)-C(2)	1.519(3)	C(13)-C(18)	1.384(2)
0(2)-C(2)	1.219(3)	C(14)-C(15)	1.378(3)
C(2)-C(3)	1.453(3)	C(15)-C(16)	1.387(3)
C(3)-C(4)	1.329(3)	C(16)-0(19)	1.364(2)
C(4)-C(4A)	1.453(3)	C(16)-C(17)	1.376(3)
C(4A)-C(5)	1.387(3)	C(17)-C(18)	1.390(3)
C(4A)-C(8A)	1.414(3)	0(19)-C(20)	1.413(3)
C(5)-C(6)	1.386(3)	C(21)-C(26)	1.393(3)
C(6)-C(7)	1.379(3)	C(21)-C(22)	1.397(2)
C(7)-C(8)	1.382(3)	C(22)-C(23)	1.376(3)
C(8)-C(8A)	1.398(3)	C(23)-C(24)	1.380(3)
N(9)-0(10)	1.395(2)	C(24)-0(27)	1.370(2)
0(10)-C(11)	1.465(2)	C(24)-C(25)	1.392(2)
C(11)-C(21)	1.519(2)	C(25)-C(26)	1.380(2)
C(11)-C(12)	1.525(2)	0(27)-C(28)	1.419(2)
C(11)-C(13)	1.528(3)		

Table 2: Bond Angles (Degrees) with Standard Deviations

N(9)-C(1)-C(8A)	129.50(16)	C(12)-C(11)-C(13)	107.38(14)
N(9)-C(1)-C(2)	110.83(16)	0(12)-C(12)-C(11)	124.49(17)
C(8A)-C(1)-C(2)	119.16(16)	C(14)-C(13)-C(18)	118.37(17)
0(2)-C(2)-C(3)	123.10(19)	C(14)-C(13)-C(11)	121.67(15)
0(2)-C(2)-C(1)	121.88(19)	C(18)-C(13)-C(11)	119.87(16)
C(3)-C(2)-C(1)	114.96(18)	C(15)-C(14)-C(13)	120.71(17)
C(4)-C(3)-C(2)	121.81(19)	C(14)-C(15)-C(16)	120.53(18)
C(3)-C(4)-C(4A)	123.21(19)	0(19)-C(16)-C(17)	124.87(17)
C(5)-C(4A)-C(8A)	119.74(18)	0(19)-C(16)-C(15)	115.65(17)
C(5)-C(4A)-C(4)	120.56(18)	C(17)-C(16)-C(15)	119.47(17)
C(8A)-C(4A)-C(4)	119.69(18)	C(16)-C(17)-C(18)	119.59(17)
C(6)-C(5)-C(4A)	120.88(18)	C(13)-C(18)-C(17)	121.32(18)
C(7)-C(6)-C(5)	119.7(2)	C(16)-0(19)-C(20)	118.37(18)
C(6)-C(7)-C(8)	120.4(2)	C(26)-C(21)-C(22)	117.63(16)
C(7)-C(8)-C(8A)	121.03(18)	C(26)-C(21)-C(11)	120.69(14)
C(8)-C(8A)-C(4A)	118.23(18)	C(22)-C(21)-C(11)	121.64(16)
C(8)-C(8A)-C(1)	124.09(16)	C(23)-C(22)-C(21)	120.92(16)
C(4A)-C(8A)-C(1)	117.69(16)	C(22)-C(23)-C(24)	120.64(15)
C(1)-N(9)-0(10)	113.28(15)	0(27)-C(24)-C(23)	116.36(15)
N(9)-0(10)-C(11)	108.44(13)	0(27)-C(24)-C(25)	124.12(16)
0(10)-C(11)-C(21)	111.17(14)	C(23)-C(24)-C(25)	119.52(16)
0(10)-C(11)-C(12)	106.08(14)	C(26)-C(25)-C(24)	119.43(16)
C(21)-C(11)-C(12)	113.61(15)	C(25)-C(26)-C(21)	121.75(15)
0(10)-C(11)-C(13)	104.39(14)	C(24)-0(27)-C(28)	117.08(14)
C(21)-C(11)-C(13)	113.54(14)		


C20
C17
C18
C21
O27
C28
C23
C24
C25
C22
C26
O12
C13
C12
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C16
C11
N9
C14
C15
O10
C1
C2
O2
C8A
C8
C3
C7
C4A
C4
C5
C6
OMe
OMe
C
HC=O
O
N
O

(171)

Figure 3

bond angles for (171) can be found in Tables 1 and 2. Comparison of the ^{1}H nmr spectra of the two crops then reveals the minor crop to be an 8:1 mixture of *syn* and *anti* isomers. It should be noted that of the signals due to aldehydic protons, that of the *anti* isomer appears at a higher frequency than the *syn* isomer, as was the case for the corresponding resonances in the ^{1}H nmr spectrum of 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [see Page 26, Scheme 25; (117) and (118)] and the di-(4-methylphenyl) compound [see Page 34, Scheme 29; (135a)].

With the dianisyl oxime ether (171) now available, its conversion to the novel potentially photochromic compound (172) was attempted. The *anti* isomer of the dianisyl oxime ether (171) was therefore heated with triphenylphosphine in 1,2-dimethoxyethane to give 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172) in good yield (62%). The naphthoxazine derivative (172) analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with its assigned structure. Having established that the synthesis of the naphthoxazine derivative (172) can be achieved through the condensation of the chloro-aldehyde (170) and the 1,2-naphthalenedione 1-oxime lithium salt (112) followed by reaction of the resulting oxime ether (171) with triphenylphosphine, the synthesis was attempted as a 'one-pot' procedure. Thus the lithium salt (112) was reacted with the chloro-aldehyde (170) at room temperature in 1,2-dimethoxyethane then the reaction mixture was treated with triphenylphosphine and heated under reflux. Reaction under these conditions

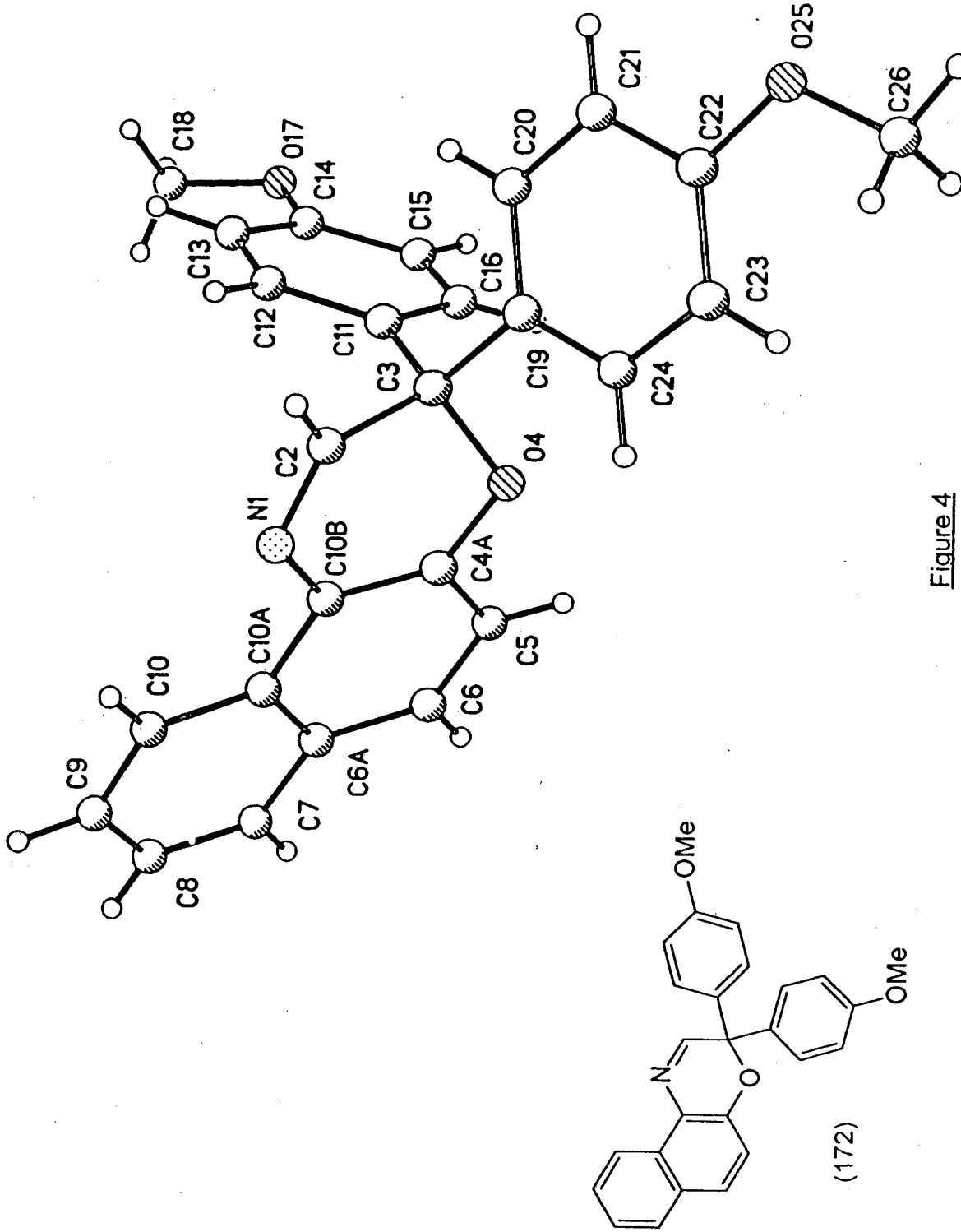
X-Ray Diffraction Data for 3,3-Di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172)

Table 3: Bond Lengths (Angstroms) with Standard Deviations

N(1)-C(2)	1.271(2)	C(10A)-C(10B)	1.424(2)
N(1)-C-(10B)	1.408(2)	C(11)-C(12)	1.380(2)
C(2)-C(3)	1.523(2)	C(11)-C(16)	1.391(2)
C(3)-0(4)	1.4584(18)	C(12)-C(13)	1.389(2)
C(3)-C(19)	1.520(2)	C(13)-C(14)	1.379(2)
C(3)-C(11)	1.525(2)	C(14)-0(17)	1.363(2)
0(4)-C(4A)	1.3731(18)	C(14)-C(15)	1.383(2)
C(4A)-C(10B)	1.370(2)	C(15)-C(16)	1.371(2)
C(4A)-C(5)	1.399(2)	0(17)-C(18)	1.412(2)
C(5)-C(6)	1.364(2)	C(19)-C(24)	1.382(2)
C(6)-C(6A)	1.415(3)	C(19)-C(20)	1.387(2)
C(6A)-C(7)	1.418(2)	C(20)-C(21)	1.380(2)
C(6A)-C(10A)	1.419(2)	C(21)-C(22)	1.375(3)
C(7)-C(8)	1.355(3)	C(22)-0(25)	1.3714(19)
C(8)-C(9)	1.400(3)	C(22)-C(23)	1.383(2)
C(9)-C(10)	1.364(2)	C(23)-C(24)	1.388(2)
C(10)-C(10A)	1.417(2)	0(25)-C(26)	1.411(3)

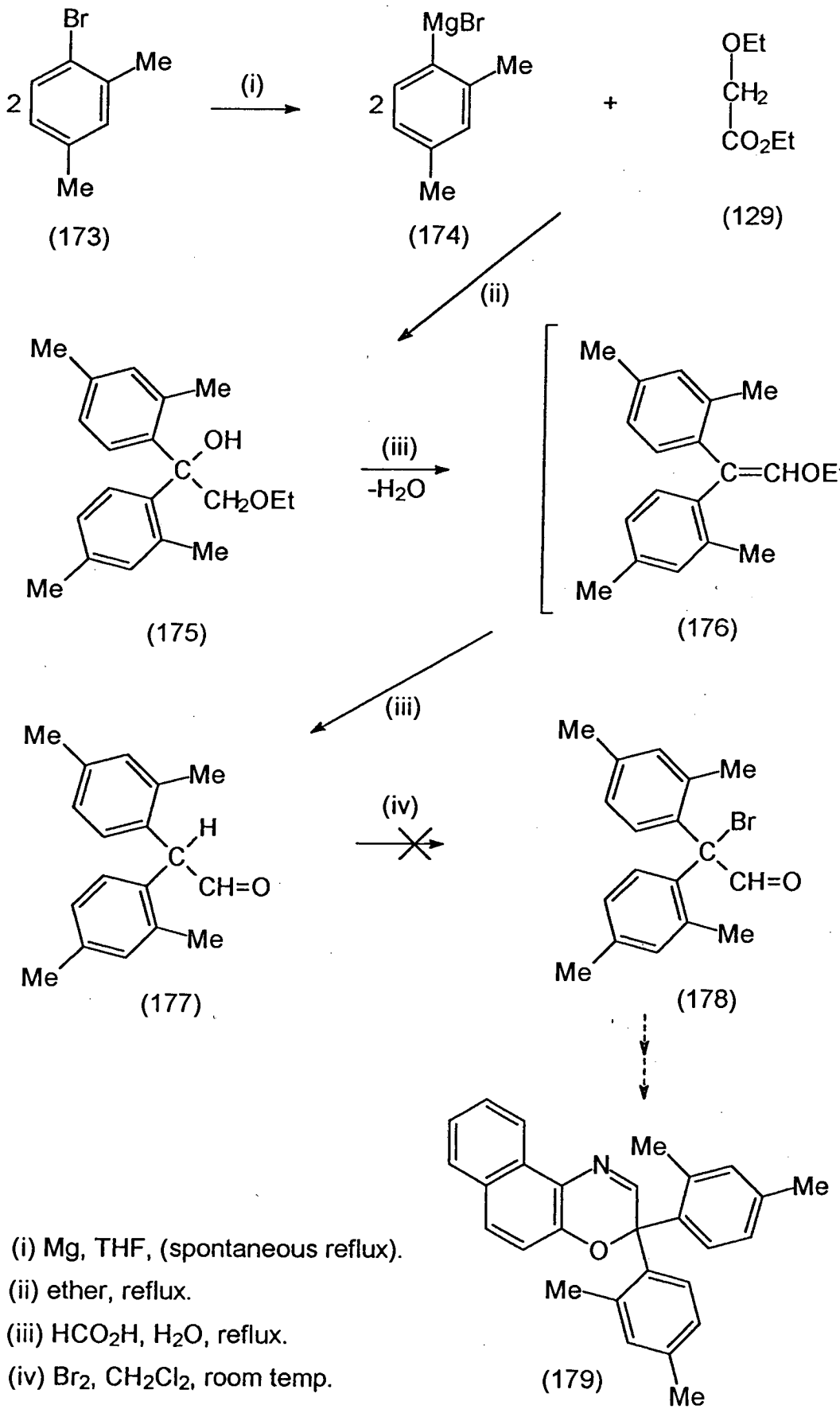
Table 4: Bond Angles (Degrees) with Standard Deviations

C(2)-N(1)-C(10B)	116.11(13)	C(4A)-C(10B)-C(10A)	119.43(14)
N(1)-C(2)-C(3)	123.91(14)	N(1)-C(10B)-C(10A)	119.69(14)
0(4)-C(3)-C(19)	105.54(12)	C(12)-C(11)-C(16)	118.16(15)
0(4)-C(3)-C(2)	106.88(12)	C(12)-C(11)-C(3)	123.13(14)
C(19)-C(3)-C(2)	110.65(12)	C(16)-C(11)-C(3)	118.69(14)
0(4)-C(3)-C(11)	107.86(12)	C(11)-C(12)-C(13)	121.15(15)
C(19)-C(3)-C(11)	113.88(13)	C(14)-C(13)-C(12)	119.70(15)
C(2)-C(3)-C(11)	111.57(12)	0(17)-C(14)-C(13)	124.65(15)
C(4A)-O(4)-C(3)	113.33(11)	0(17)-C(14)-C(15)	115.82(15)
C(10B)-C(4A)-O(4)	119.90(13)	C(13)-C(14)-C(15)	119.52(16)
C(10B)-C(4A)-C(5)	122.33(14)	C(16)-C(15)-C(14)	120.35(16)
O(4)-C(4A)-C(5)	117.63(13)	C(15)-C(16)-C(11)	121.01(15)
C(6)-C(5)-C(4A)	118.89(16)	C(14)-0(17)-C(18)	117.65(14)
C(5)-C(6)-C(6A)	121.48(16)	C(24)-C(19)-C(20)	118.09(14)
C(6)-C(6A)-C(7)	122.23(17)	C(24)-C(19)-C(3)	120.80(14)
C(6)-C(6A)-C(10A)	119.11(15)	C(20)-C(19)-C(3)	121.07(14)
C(7)-C(6A)-C(10A)	118.66(17)	C(21)-C(20)-C(19)	121.03(16)
C(8)-C(7)-C(6A)	120.68(19)	C(22)-C(21)-C(20)	120.22(16)
C(7)-C(8)-C(9)	120.78(17)	0(25)-C(22)-C(21)	116.12(15)
C(10)-C(9)-C(8)	120.41(18)	0(25)-C(22)-C(23)	124.07(16)
C(9)-C(10)-C(10A)	120.54(18)	C(21)-C(22)-C(23)	119.81(15)
C(10)-C(10A)-C(6A)	118.85(15)	C(22)-C(23)-C(24)	119.45(16)
C(10)-C(10A)-C(10B)	122.48(15)	C(19)-C(24)-C(23)	121.37(15)
C(6A)-C(10A)-C(10B)	118.67(15)	C(22)-0(25)-C(26)	117.29(15)
C(4A)-C(10B)-N(1)	120.64(14)		


C18
O17
C14
C15
C13
C16
C12
C11
C3
C19
C20
C21
C22
O25
C26
C23
C24
O4
C2
N1
C10B
C4A
C10A
C5
C10
C6
C9
C6A
C7
C8
OMe
OMe
N
O

(172)

Figure 4



(i) Mg, THF, (spontaneous reflux).

(ii) ether, reflux.

(iii) HCO_2H, H_2O, reflux.

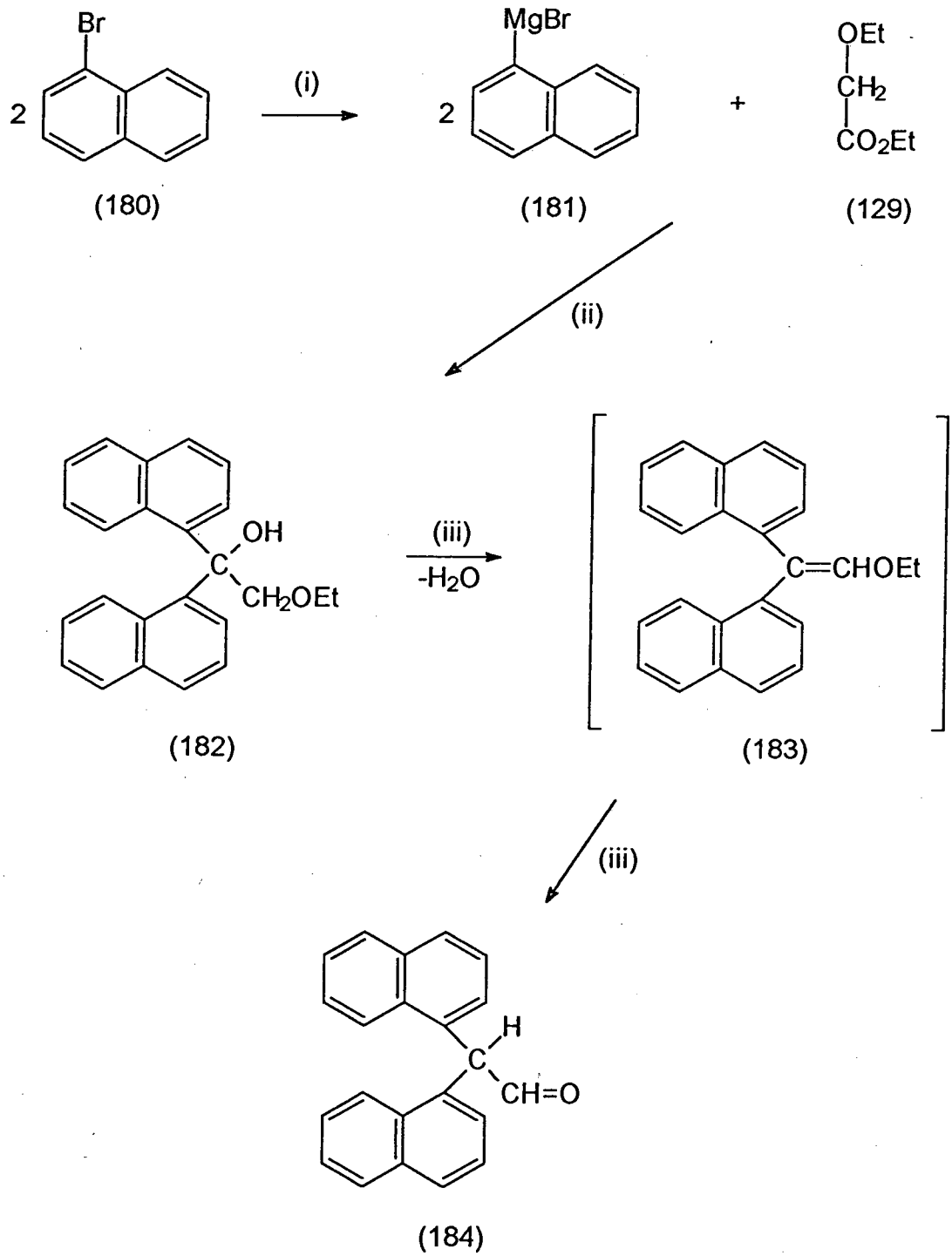
(iv) Br_2, CH_2Cl_2, room temp.

Scheme 40

gave the naphthoxazine derivative (172) in good yield (68%). A single crystal of 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172) was submitted for X-ray diffraction analysis, the result of which is shown in Figure 4, (see Page 57). The corresponding bond lengths and bond angles are displayed in Tables 3 and 4.

Having finally synthesised the dianisylnaphthoxazine derivative (172), studies were continued on the synthesis of further diarylnaphthoxazines. The next target to be chosen (Scheme 40) was the di-(2,4-dimethylphenyl)naphthoxazine derivative (179). On first examination, the ortho substitution of the aryl substituents of (179) would be expected to affect the photochromic characteristics of the molecule in a similar manner to para substitution. However, Van Gemert[68] observes that such ortho substitution of the aryl substituents of a diarylnaphthopyran unexpectedly dramatically enhances the optical density of the photoproduct and slows the fade rate. These observations provided the stimulus for the attempted synthesis of (179).

In keeping with previous syntheses, attempts were first made to synthesise the corresponding bromo-aldehyde, 2-bromo-2,2-di-(2,4-dimethylphenyl)-acetaldehyde (178). Thus, 2,4-dimethylbromobenzene (173) was treated with magnesium in tetrahydrofuran and the resulting Grignard reagent (174) was heated with ethyl 2-ethoxyacetate (129) in ether. Under these conditions a product was isolated in good yield (76%) whose combustion analysis and ir and ^{1}H nmr spectra are consistent with its formulation as the ether-alcohol

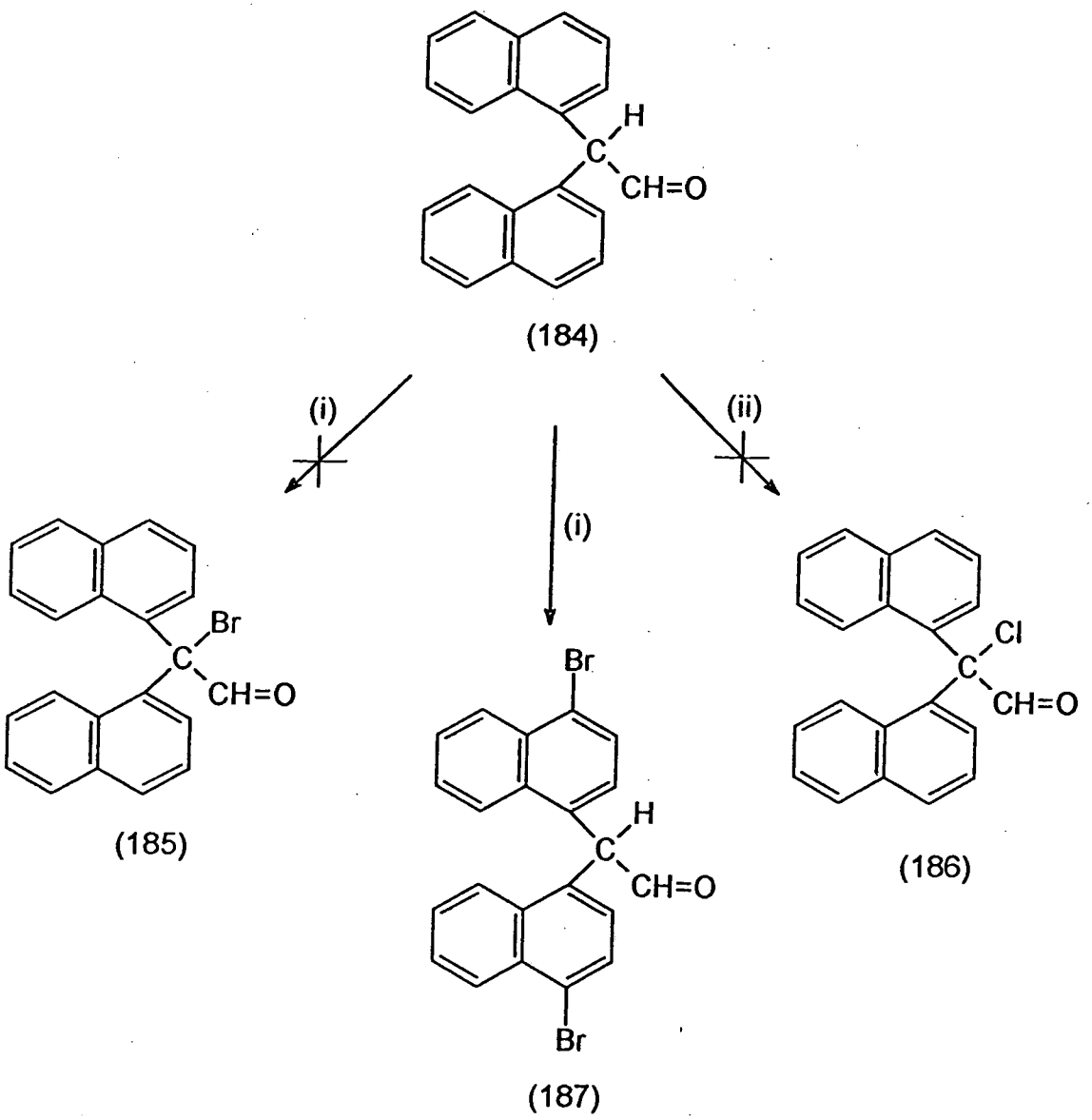


(i) Mg, THF, (spontaneous reflux).

(ii) ether, reflux.

(iii) HCO_2H, H_2O, reflux.

Scheme 41



(i) Br_2, CH_2Cl_2, room temp.

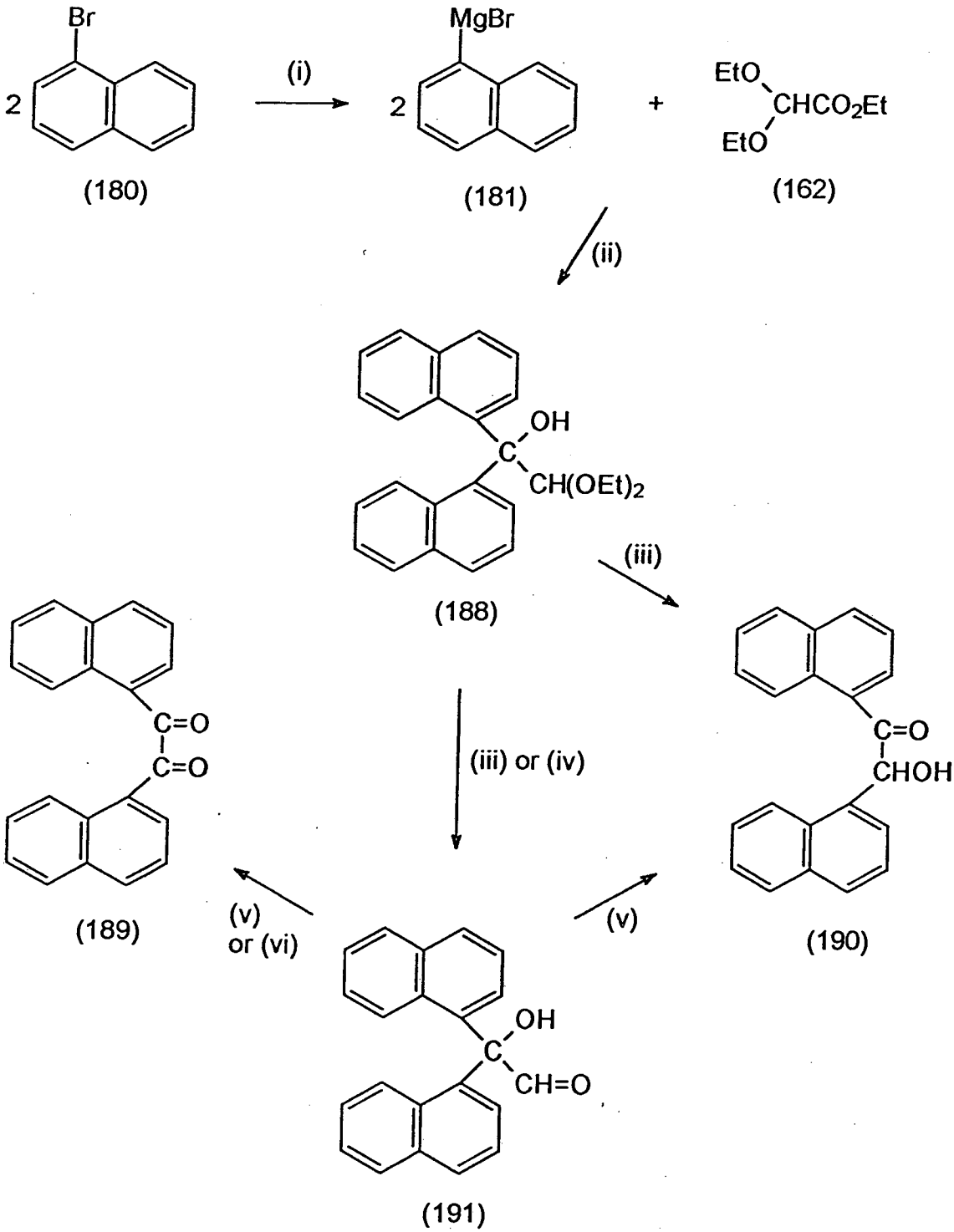
(ii) SO_2Cl_2, CH_2Cl_2, -10°C.

Scheme 42

(175). With the ether-alcohol (175) available, its cleavage by treatment with hot aqueous formic acid to give the aldehyde (177) was attempted. Distillation of the crude product of this reaction afforded the aldehyde (177) as a colourless oil in excellent yield (87%). The bromination of the 2,2-di-(2,4-dimethylphenyl)acetaldehyde (177) was next attempted. Unfortunately, reaction with bromine at room temperature in dichloromethane gave a complex mixture, possibly due to bromination of the aromatic rings taking place. Under these conditions no product suitable for use as a starting material in the synthesis of the naphthoxazine derivative (179) was isolated. Rather than pursue further routes to 3,3-di-(2,4-dimethylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (179), focus was switched to alternative photochromic structures.

The synthesis (Scheme 41) of 2,2-di-(naphth-1-yl)acetaldehyde (184) and (Scheme 42) its bromo derivative (185) was next attempted with the aim of gaining access to novel di-(naphth-1-yl)naphthoxazine derivatives. Thus (Scheme 41), 1-naphthylmagnesium bromide (181) was prepared then heated with ethyl 2-ethoxyacetate (129) in ether to give a moderate yield (64%) of a product whose combustion analysis and ir and ^{1}H nmr spectra support its formulation as the ether-alcohol (182). Solvolysis of the ether-alcohol (182) was achieved efficiently (78%) using hot aqueous formic acid, and then bromination of the resulting di-(naphth-1-yl)acetaldehyde (184) was investigated. Reaction (Scheme 42) of the aldehyde (184) with three equivalents of bromine in dichloromethane at room temperature afforded a good yield (72%) of a solid product, the combustion analysis of which indicated

that dibromination had taken place. Closer examination of the ir, ^{1}H and ^{13}C nmr spectra of the dibrominated product (187) reveals that bromination occurred in the naphthalene rings more readily than at the α-position which remains unreacted. Thus, the ^{1}H nmr spectrum shows a pair of one-proton doublets at δ_H 10.19 and 6.31 attributable to the aldehyde and methine groups respectively, similarly the ^{13}C nmr spectrum shows signals due to CH groups at δ_C 198.0 and 56.0. Both the carbon and proton nmr spectra show the expected signals due to the monobrominated naphthalene rings, and on closer inspection, an attempt to assign the positions of the bromine atoms can be made. The ^{1}H spectrum reveals two simple doublets (δ_H 7.72 and 7.01, J 7.8 Hz) due to ortho coupled protons which are not coupled to any of the other hydrogens. This coupling would not be observed had bromination occured in the left-hand rings (positions 5-8) of the naphth-1-yl moieties. To account for this ortho coupling, substitution must have occurred in the 2- or 4- positions of the of the naphthalene rings. Bromination at the 4- position is considered the most likely of these two possibilities though unequivocal formulation of the dibromo compound as (187) is not claimed. In an attempt to establish whether reaction with excess bromine would afford a single polybrominated product suitable for use as a starting material for the synthesis of di-(naphth-1-yl)naphthoxazine derivatives, the aldehyde (184) was treated with eight equivalents of bromine at room temperature in dichloromethane. The ^{1}H and ^{13}C nmr spectra of the product of this reaction indicate that while bromination at the α-position of the aldehyde had been achieved, shown by the absence of



(i) Mg, THF, (spontaneous reflux).

(ii) ether, reflux.

(iii) 2M HCl(aq), dioxane, reflux.

(iv) 2M HCl(aq), DME, reflux.

(v) HBr(g), $CaCl_2$, ether, 0°C to room temp.

(vi) HCl(g), $CaCl_2$, ether, 0°C to room temp.

Scheme 43

signals at δ_H 6.31 and δ_C 56.0, a number of products were present which proved to be inseparable. In an alternative approach, an attempt was made to synthesise the α-chloro-aldehyde (185). However, on treatment of the aldehyde (184) with sulphuryl chloride at -10°C in dichloromethane, no chlorination occurred. Repetition of the attempted chlorination under reflux in dichloromethane also afforded a quantitative yield of unreacted aldehyde (184).

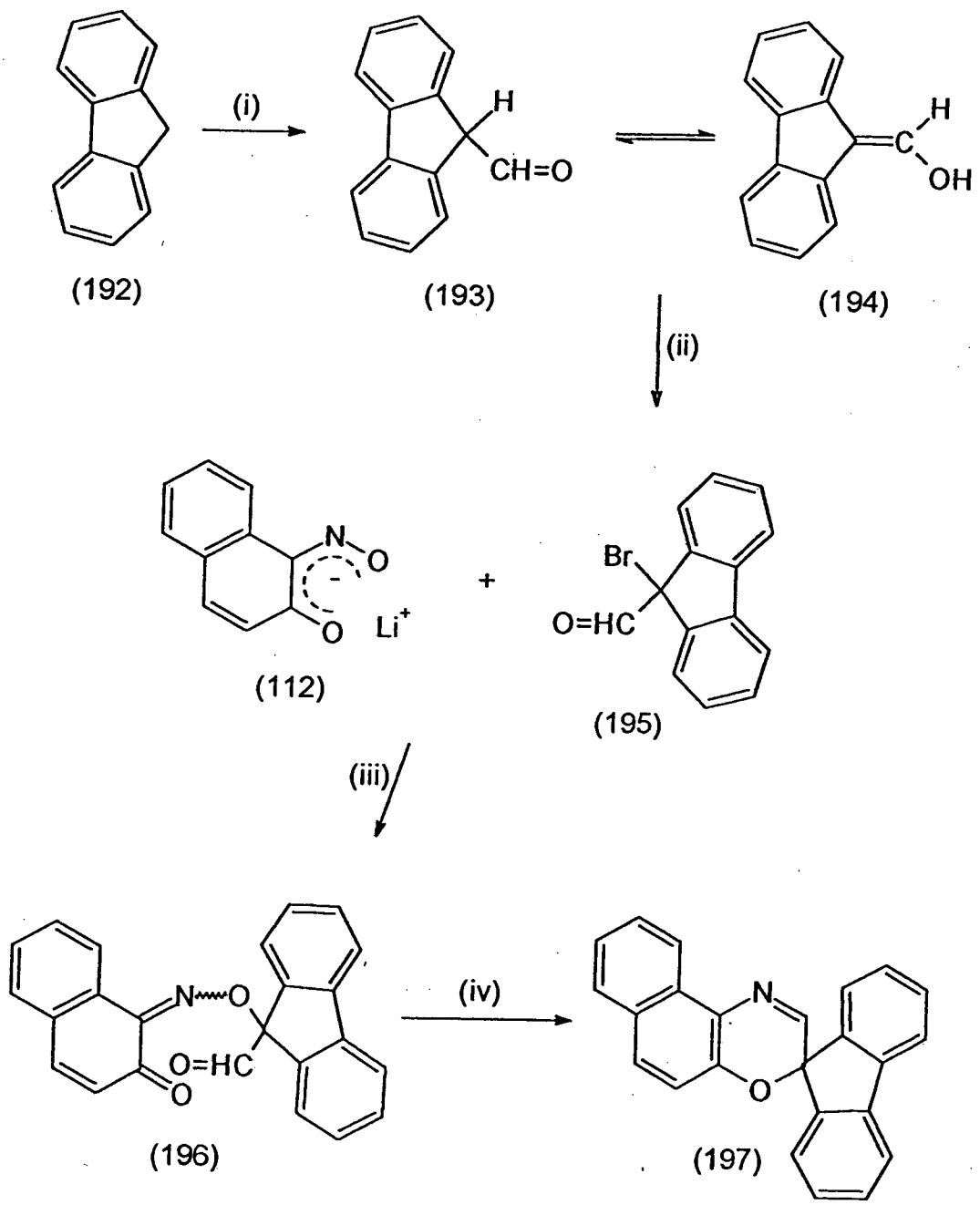
Having encountered difficulties in the halogenation of the di-(naphth-1-yl)acetaldehyde (184) alternative routes to α-halogeno di-(naphth-1-yl)acetaldehydes were investigated. Problems encountered in the halogenation of the di-(4-methoxyphenyl)acetaldehyde [see Page 43, Scheme 28; (133d)] were solved through the synthesis of the α-hydroxy derivative [see Page 50, Scheme 38; (169)] and its reaction with hydrogen chloride gas. The application of this methodology to the synthesis of 2-chloro-2,2-di-(naphth-1-yl)acetaldehyde (186) was therefore attempted. Thus (Scheme 43), the naphthylmagnesium bromide (181) was heated with ethyl 2,2-diethoxyacetate (162) in ether giving the dinaphthyl hydroxy-acetal (188) in good yield (63%). The mass spectrum of the hydroxy-acetal (188) gives no parent ion, but shows a peak corresponding to a di-(naphth-1-yl)hydroxymethyl cation while its ir spectrum gives the expected hydroxyl absorption band (ν_{max} 3485 cm^{-1}). In the ^1H nmr spectrum, the methylene groups of the ethoxy moieties are non-equivalent while the methyl groups are coincident. Furthermore, typical splitting patterns for ethyl groups are not observed. The methylene groups

give rise to broad singlets (δ_H 3.80-3.50 and 3.20-2.90) while the methyl groups give rise to a broad six-proton singlet (δ_H 1.10-0.90). The diastereotopic nature of the protons of the methylene groups accounts for their non-equivalence in the ^{1}H nmr spectrum. This phenomenon was also observed in the case of the diphenyl compound [see Scheme 34; (52)]. The dinaphthyl hydroxy-acetal (188) is a sterically crowded structure and the resulting rotational restrictions account for the broadening of the signals due to the ethoxy groups.

With the dinaphthyl hydroxy-acetal (188) available its hydrolysis to the hydroxy-aldehyde (191) was attempted. Treatment of the hydroxy-acetal (188) with dilute aqueous hydrochloric acid in refluxing 1,4-dioxane afforded a moderate yield (53%) of 2,2-di-(naphth-1-yl)-2-hydroxyacetaldehyde (191) which analysed correctly and exhibits mass, ir and ^{1}H nmr spectroscopic properties fully in accord with its assigned structure. Also isolated from this reaction was a poor yield (34%) of 1,2-di-(naphth-1-yl)-2-hydroxy-1-oxoethane (190) whose mass, ir and ^{1}H nmr spectra support its assigned structure. Thus, the ir spectrum shows absorption bands due to the hydroxyl (ν_{max} 3168 cm^{-1}) and carbonyl (ν_{max} 1673 cm^{-1}) groups, while the ^{1}H nmr spectrum shows signals due to the aromatic protons, a one-proton doublet (δ_H 4.74) attributable to the hydroxyl group which is removed on shaking with deuterium oxide and a one-proton doublet (δ_H 6.72) due to the methine group which collapses to a singlet on treatment with deuterium oxide. The formation of the benzoin-type structure (190) is directly analogous to the previously described formation of

4,4'-dimethoxybenzoin [see Page 52, Scheme 38; (168)] and may be due to a pinacol-type rearrangement of the hydroxy-aldehyde (191). On repetition of the hydrolysis an attempt was made to prevent the formation of the unwanted (190) by simply reacting the corresponding hydroxy-acetal (188) with dilute aqueous hydrochloric acid at room temperature in 1,4-dioxane. However, reaction under these conditions afforded only unreacted hydroxy-acetal (188) in moderate yield (65%). On the other hand, repetition of this reaction using dilute hydrochloric acid in refluxing 1,2-dimethoxyethane afforded an excellent yield (91%) of the desired dinaphthyl hydroxy-aldehyde (191).

The chlorination of the hydroxy-aldehyde (191) was next investigated. However, saturation of an ether solution of the hydroxy-aldehyde (191) with hydrogen chloride in the presence of calcium chloride at 0°C to room temperature gave a mixture from which a poor yield (45%) of 1,2-di-(naphth-1-yl)-2-hydroxy-1-oxoethane (190) was isolated together with 1,2-di-(naphth-1-yl)-1,2-dioxoethane (189) (27%). As the poor solubility of the hydroxy-aldehyde (191) in ether had required large volumes to be used for the attempted chlorination, 1,2-dimethoxyethane was chosen as the solvent for the analogous reaction with hydrogen bromide. However, reaction of the hydroxy-aldehyde (191) with hydrogen bromide in the presence of calcium chloride at 0°C to room temperature gave only a small amount of the diketone (189) and none of the desired bromo-aldehyde [Scheme 42; (185)]. Studies on the synthesis of di-(naphth-1-yl)naphthoxazine derivatives were terminated at this point.



(i) NaH, HCO_2Et, ether, reflux then 20% v/v H_2SO_4(aq), 0°C.

(ii) Br_2, CH_2Cl_2, room temp.

(iii) acetone, room temp.

(iv) Ph_3P, THF or dioxane, reflux.

Scheme 44

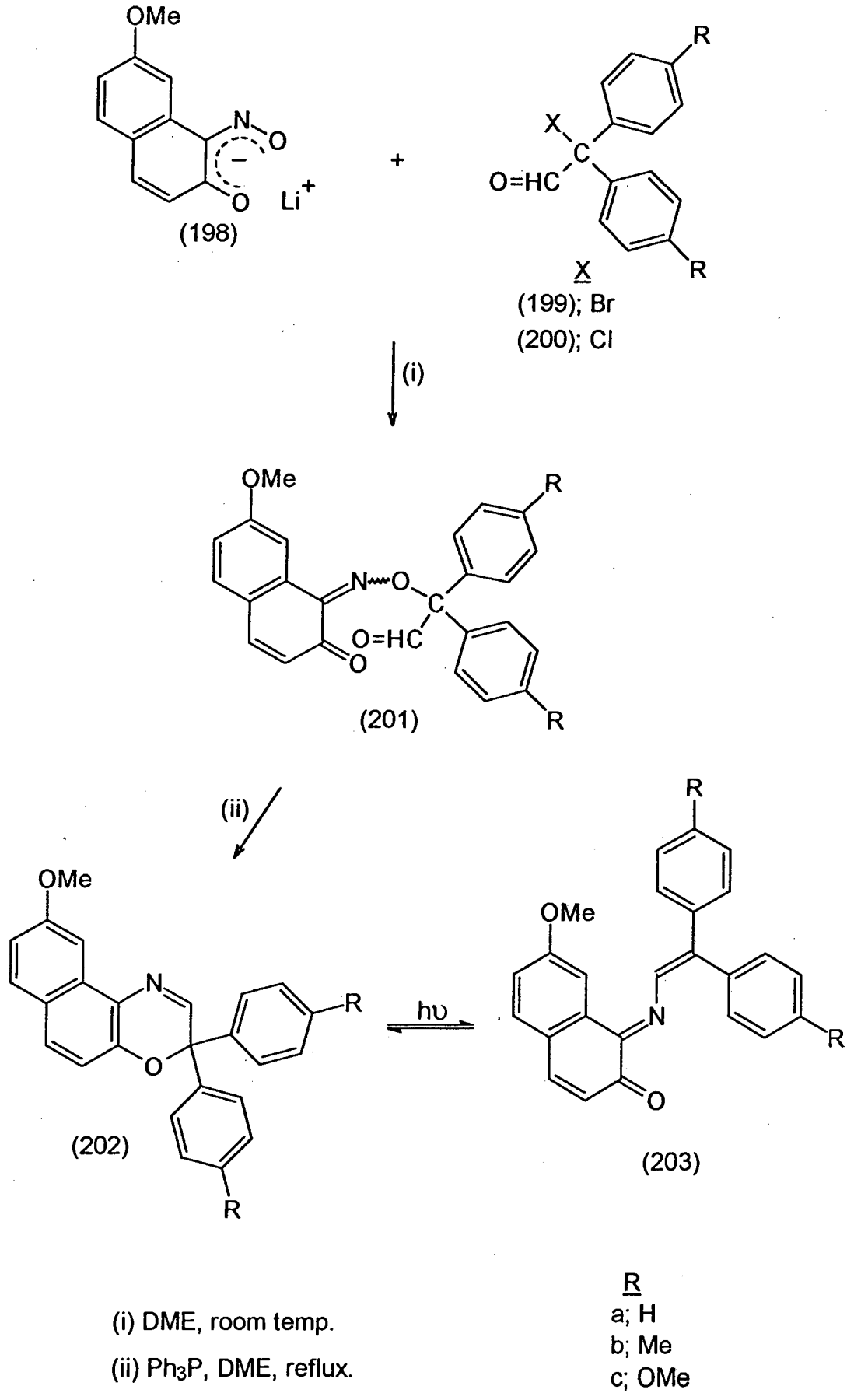
Work was next undertaken to synthesise (Scheme 44) the previously reported[139] but poorly described photochromic 3,3-spirofluoren-9-yl-3*H*-naphth[2,1-*b*]-1,4-oxazine (197). The photochromic characteristics of this compound are not known though it may be expected to behave as a diphenyl compound whose phenyl substituents are both ortho substituted. Initial investigations involved the two step synthesis of the unknown 9-bromofluorene-9-carboxaldehyde (195) and the study of its condensation with the 1,2-naphthalenedione 1-oxime lithium salt (112). It was hoped that the resulting fluorenyl oxime ether (196) would then cyclise on reaction with triphenylphosphine to give the naphthoxazine derivative (197). The known[149] fluorene-9-carboxaldehyde (193) was readily prepared through formylation of the anion of fluorene (192) with ethyl formate. Under these conditions a yellow solid product was isolated in high yield (90%) whose mass and ir spectra are consistent with its formulation as fluorene-9-carboxaldehyde (193). The tautomerism of the aldehyde [(193) $\rightleftharpoons$ (194)] is well understood[150] and its ir spectrum shows absorption bands at ν_{max} 2825 and 1715 cm^{-1} due to the aldehyde group and a band at ν_{max} 3500-3100 cm^{-1} due to the hydroxy group of the enol form. With the fluorenyl aldehyde (193) available, its bromination was investigated. Treatment of a dichloromethane solution of the aldehyde (193) with bromine at room temperature gave a good yield (73%) of a cream solid product whose formulation as the bromo-aldehyde (195) is fully supported by its analytical and spectroscopic properties.

The condensation of the bromo-aldehyde (195) with 1,2-naphthalenedione 1-oxime lithium salt (112) was attempted at room temperature in acetone. The resulting yellow solid product, isolated in good yield (68%), analysed correctly and has mass, ir and ^{1}H nmr spectral properties consistent with it being 1,2-naphthalenedione 1-oxime 9-formylfluoren-9-yl ether (196). Thus, the ir spectrum shows the expected carbonyl absorption bands at ν_{max} 1734 and 1662 cm^{-1} and the ^{1}H nmr spectrum shows a one-proton singlet at δ_H 9.68 attributable to the aldehyde group and two one-proton doublets at δ_H 7.12 and 6.83 due to the olefinic protons at the C_3 and C_4 positions of the naphthalene ring, as well as signals due to the aromatic protons. The ^{1}H nmr spectrum of the oxime ether (196) indicates the presence of only one isomer. As crystals suitable for X-ray analysis could not be obtained, the geometry of the oximino functionality remains undefined.

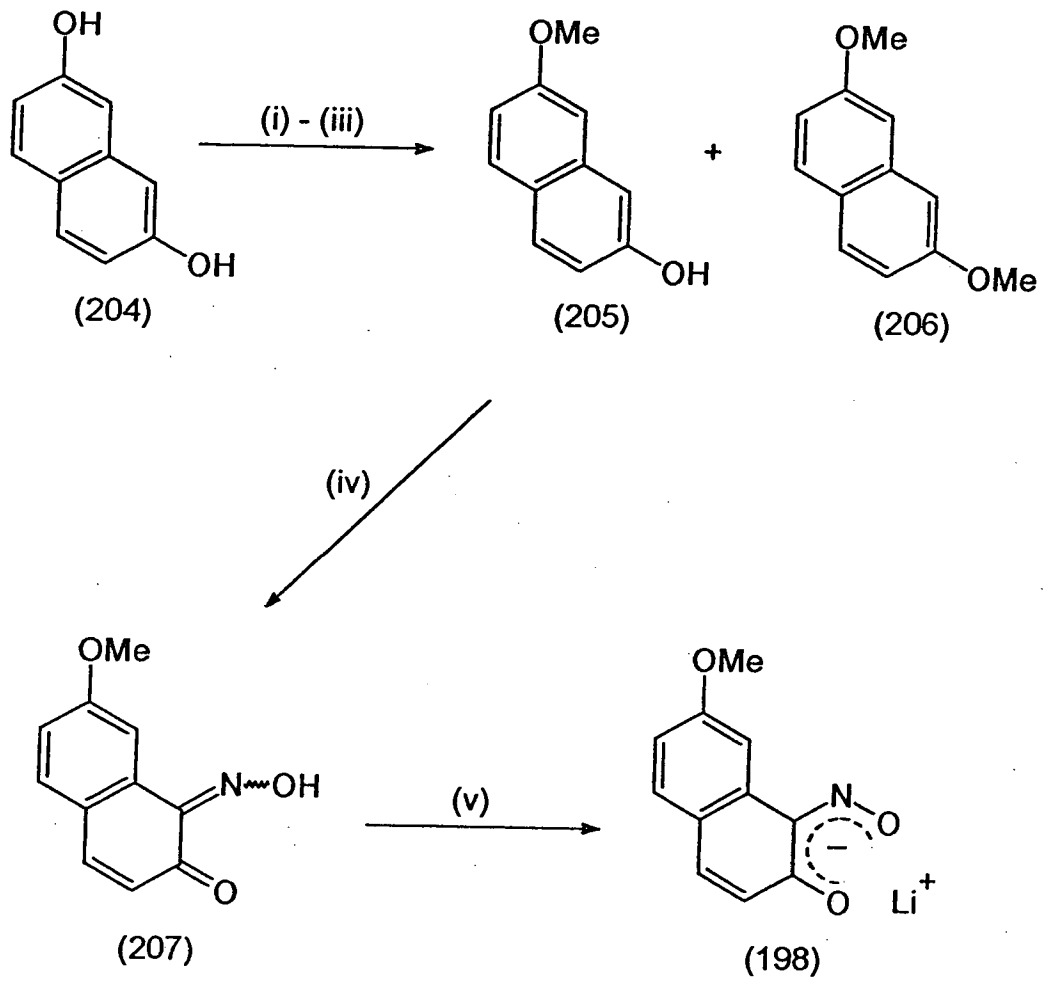
The reaction of the oxime ether (196) with triphenylphosphine was next attempted with the aim of accessing the spirofluorenylnaphthoxazine derivative (197). Unfortunately, reaction of (196) with triphenylphosphine in refluxing 1,2-dimethoxyethane gave only intractable gums. Heating the oxime ether (196) with triphenylphosphine in tetrahydrofuran afforded the desired naphthoxazine derivative (197) in very poor yield (12%). Repetition of this reaction in refluxing 1,4-dioxane gave a slightly improved yield (27%) of the photochromic naphthoxazine derivative (197). The naphthoxazine derivative (197) analysed correctly and gave mass, ir and ^{1}H nmr spectroscopic data consistent with its assigned structure.

The thermal behaviour of the fluorenyl oxime ether (196) in the absence of triphenylphosphine was also investigated. Thermolysis of the oxime ether (196) in methanol gave a good yield (73%) of a product which gave a combustion analysis indicating it to be an isomer of the starting material and whose ir and ^{1}H nmr spectra are consistent with it being an oxime ether. Thus the ir spectrum shows carbonyl absorption bands at ν_{max} 1731 and 1660 cm^{-1} and the ^{1}H nmr spectrum shows a one-proton singlet at δ_H 9.67 attributable to the aldehyde group and a one-proton doublet δ_H 6.37 due to one of the olefinic protons (C_3-C_4 of the naphthalene ring) as well as multiplets containing signals due to the remaining naphthalene protons and the fluorenyl moiety. Previously in this chapter, in cases where X-ray diffraction studies have not been possible, the structures of isomeric oxime ethers have been tentatively assigned by comparison of their ^{1}H nmr spectra with those of 1,2-naphthalenedione 1-oxime diphenylformyl ether [see Page 26, Scheme 25; (117) and (118)]. The basis for this assignment has been the higher frequency of the signal due to the aldehydic proton of the *anti* isomer (118) than that due to the *syn* isomer (117). However, in this case the isomeric fluorenyl oxime ethers (196) give signals due to their aldehydic protons which are almost coincident (δ_H 9.68 and 9.67) and consequently no assignment of their geometries is attempted.

As has previously been described, electron-donating para substituents on the phenyl groups of 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazine [see Page 31, Scheme 29; (137)] would be expected to affect the colour, intensity and fade of


OMe
N
O
O
Li+
(198)
+
R
X
C
O=HC
X
R
(199); Br
(200); Cl
(i)
OMe
R
N
O
C
O=HC
O
(201)
R
(ii)
OMe
N
O
R
(202)
R
hυ
R
OMe
N
O
R
(203)
(i) DME, room temp.
(ii) Ph3P, DME, reflux.
R
a; H
b; Me
c; OMe

Scheme 45



(i) NaH, DMF, 10°C then Me_2SO_4, 100°C.
(ii) K_2CO_3, Me_2SO_4, acetone, room temp. or reflux.
(iii) K_2CO_3, MeI, acetone, room temp.
(iv) $NaNO_2$, AcOH, H_2O, 10°C to room temp.
(v) LiOH, acetone, H_2O, room temp.

Scheme 46

the photochromic compound, such expectations being based on observations of the analogous naphthopyrans.[68] By analogy with observations of spirooxazine compounds[82] it was expected that the presence of electron-donating substituents on the naphthalene nucleus would also affect the photochromism of (137). It has been reported[82] that the presence of a methoxy group at the 9'-position of the spirooxazine derivative [see Page 12, Scheme 12; (58)] improves the photochromic response of the compound though has little effect on the visible absorption band. A further possible effect of substitution in the 9-position of a 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 45; (202)] is a change in the compound's fade kinetics, a property which must be considered when assessing the suitability of any photochromic agent for a given application. It is possible that substitution at the 9-position would give rise to a kinetic effect due to the close proximity of the methoxy group to the diaryl portion of the molecule in the *anti*-quinonoidal ring-opened form (203). The resulting steric destabilisation may cause a more rapid reversion of the open chain form (203) to the bleached state (202).

With these considerations in mind, work was undertaken (Scheme 45) to prepare the lithium salt (198) of 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198). It was hoped (Scheme 46) that mono-methylation of commercially available 2,7-dihydroxynaphthalene (204) and nitrosation of the resulting known[151] 7-methoxy-2-naphthol (205) would afford the known[151] 7-methoxy-1,2-naphthalenedione 1-oxime (207). Preparation of the lithium salt (198) of the methoxynaphthalenedione oxime (207) followed by its

condensation (Scheme 45) with a 2-halogeno-2,2-diarylacetaldehyde [(199) or (200)] would then afford the oxime ether (201) precursors to the desired naphthoxazine derivatives (202). Thus 2,7-dihydroxynaphthalene (204) was treated with sodium hydride in dimethylformamide then heated with dimethyl sulphate at 100°C. Methylation under these conditions gave a mixture, flash-chromatography of which afforded the methoxynaphthol (205) in poor yield (29%) and 2,7-dimethoxynaphthalene (206) also in poor yield (18%). In an attempt to improve the yield of the monomethylated product (205), the diol (204) was treated with 0.6 equivalents of potassium carbonate then heated with dimethyl sulphate in acetone. Under these conditions the desired methoxynaphthol (205) was isolated in poor yield (40%) together with the dimethoxynaphthalene (206) (31%) and unreacted 2,7-dihydroxynaphthalene (204) (14%). Repetition of this reaction using an excess (1.3 equivalents) of potassium carbonate gave similar yields of 7-methoxy-2-naphthol (205) (37%) and 2,7-dimethoxynaphthalene (206) (29%). In a parallel approach, an acetone solution of 2,7-dihydroxynaphthalene (204) was treated at room temperature with potassium carbonate and an alternative methylating agent methyl iodide. The methoxynaphthol (204) was isolated from this reaction in poor yield (34%) together with 2,7-dimethoxynaphthalene (205) (16%) and unreacted 2,7-dihydroxynaphthalene (204) (19%).

With the required methoxynaphthol (205) available, albeit in disappointing yield, its nitrosation was investigated. Treatment of 7-methoxy-2-naphthol (205) with sodium nitrite in aqueous acetic acid at 10°C to room temperature

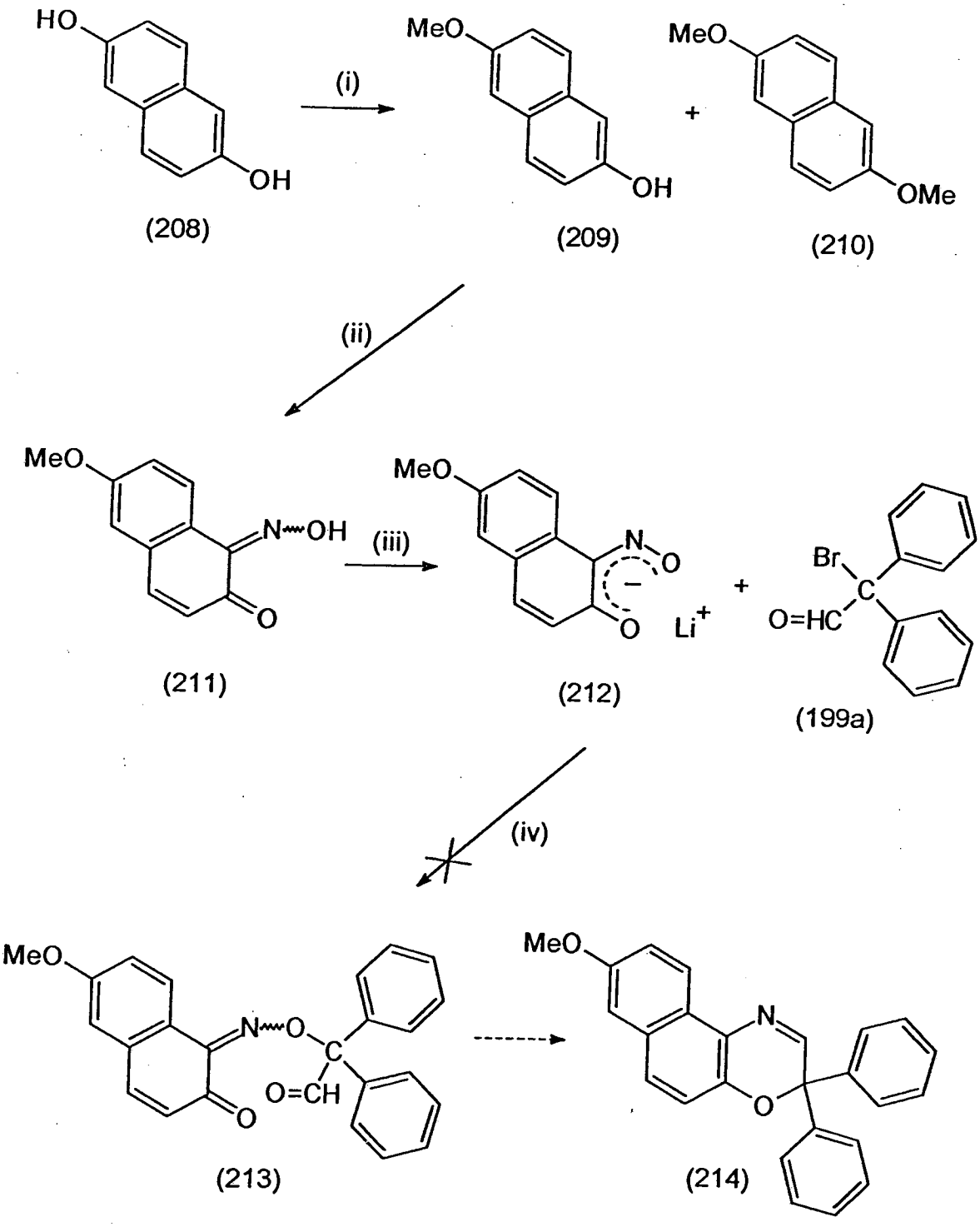
gave the 7-methoxy-1,2-naphthalenedione 1-oxime (207) in good yield (74%). An acetone solution of the methoxynaphthalenedione oxime (207) was then treated with aqueous lithium hydroxide at room temperature. The high-melting solid product of this reaction was tentatively formulated as the lithium salt (198) though attempts to purify and characterise it gave inconsistent results. The product believed to be the lithium salt (198) was found to condense (Scheme 45) as expected with 2-bromo-2,2-diphenylacetaldehyde (199a) at room temperature in 1,2-dimethoxyethane. The resulting 7-methoxy-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (201a), isolated in good yield (81%) analysed correctly and has mass, ir and ^{1}H nmr spectroscopic properties consistent with its assigned structure. Thus, the ir spectrum shows the expected carbonyl absorption bands at ν_{max} 1734 and 1665 cm^{-1}. The ^{1}H nmr spectrum, shows two singlets due to aldehydic protons (δ_H 10.07 and 9.95) and two singlets due to methoxy groups (δ_H 3.79 and 3.78) as well as signals due to the naphthyl and phenyl rings. These observations can be explained by the existence of *syn* and *anti* isomers of the oxime ether (201a). The structural assignment of the *syn* and *anti* isomers must again be based on the analogy with the 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [see Page 26, Scheme 25; (117), (118)]. Attributing the more deshielded aldehydic proton to the *anti* isomers of the oxime ether (201) the mixture can be described as a 1:5 mixture of the *syn* and *anti* isomers respectively. The cyclisation of the oxime ether (201) to the 9-methoxynaphthoxazine derivative (202) was next attempted. The mixture of *syn* and *anti* isomers of (201a) was heated with triphenylphosphine in 1,2-dimethoxyethane. Under these

conditions a photochromic product was isolated in excellent yield (91%) whose analytical and spectroscopic properties fully support its formulation as 3,3-diphenyl-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202a).

Having synthesised the 3,3-diphenyl-9-methoxynaphthoxazine derivative (202a), work was undertaken to synthesise the analogous 3,3-di-(4-methylphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202b). It was expected that the previously described 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (199b) would also condense with the methoxynaphthalenedione lithium salt (198) to give an oxime ether (201b) suitable for further elaboration to the naphthoxazine derivative (202b). The lithium salt (198) reacted with the di-(4-methylphenyl) bromo-aldehyde (199b) at room temperature in 1,2-dimethoxyethane but gave a poor yield (31%) of the desired 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methylphenyl)-formylmethyl ether (201b). The oxime ether (201b) analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with its assigned structure. The ir spectrum shows the expected carbonyl absorptions ν_{max} 1731 and 1660 cm^{-1} while the ^{1}H nmr spectrum shows a one-proton singlet at δ_H 10.01 attributable to the aldehyde group, a three-proton singlet (δ_H 3.81) due to the methoxy group and a six-proton singlet (δ_H 2.34) assignable to the methyl groups. As the ^{1}H nmr spectrum of oxime ether (201b) indicates that it was isolated as a single isomer, assignment of *syn* or *anti* geometry to this product is not possible. Also isolated from this reaction were unreacted lithium salt (198) (28%) and 7-methoxy-1,2-naphthalenedione 1-oxime (207) (6%).

The cyclisation of the oxime ether (201b) was next attempted using triphenylphosphine in refluxing 1,2-dimethoxyethane. The photochromic product of this reaction, isolated in moderate yield (62%), gave a correct combustion analysis and spectroscopic properties which fully support its formulation as 3,3-di-(4-methylphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202b).

The 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198) was also used as a starting material in the synthesis of 3,3-di-(4-methoxyphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202c). The lithium salt (198) was reacted with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (200c) at room temperature in 1,2-dimethoxyethane giving 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methoxyphenyl)formylmethyl ether (201c) in moderate yield (65%). The oxime ether (201c) gave a combustion analysis and mass and ir spectra consistent with its assigned structure while its ^{1}H nmr spectrum shows that it exists as a 1:1 mixture of two isomers which could not subsequently be separated. Thus the ir spectrum shows absorption bands at ν_{max} 2710 and 1735 cm^{-1} attributable to the aldehyde group and a further absorption band at ν_{max} 1645 cm^{-1} due to the quinone carbonyl group . The ^{1}H nmr spectrum of the oxime ether (201c) shows singlets due to aldehydic protons at δ_H 9.98 and 9.86 as well as the expected signals due to the aromatic protons and four singlets (δ_H 3.83, 3.81, 3.80 and 3.79) due to methoxy groups. The existence of two isomers of the oxime ether is once again due to *syn* and *anti* geometries of the oximino functionality and it is once again postulated that the more deshielded



(i) NaH, Me_2SO_4, DMF, room temp. or 100°C.

(ii) $NaNO_2$, AcOH, H_2O, 10°C to room temp.

(iii) LiOH, H_2O, acetone, room temp.

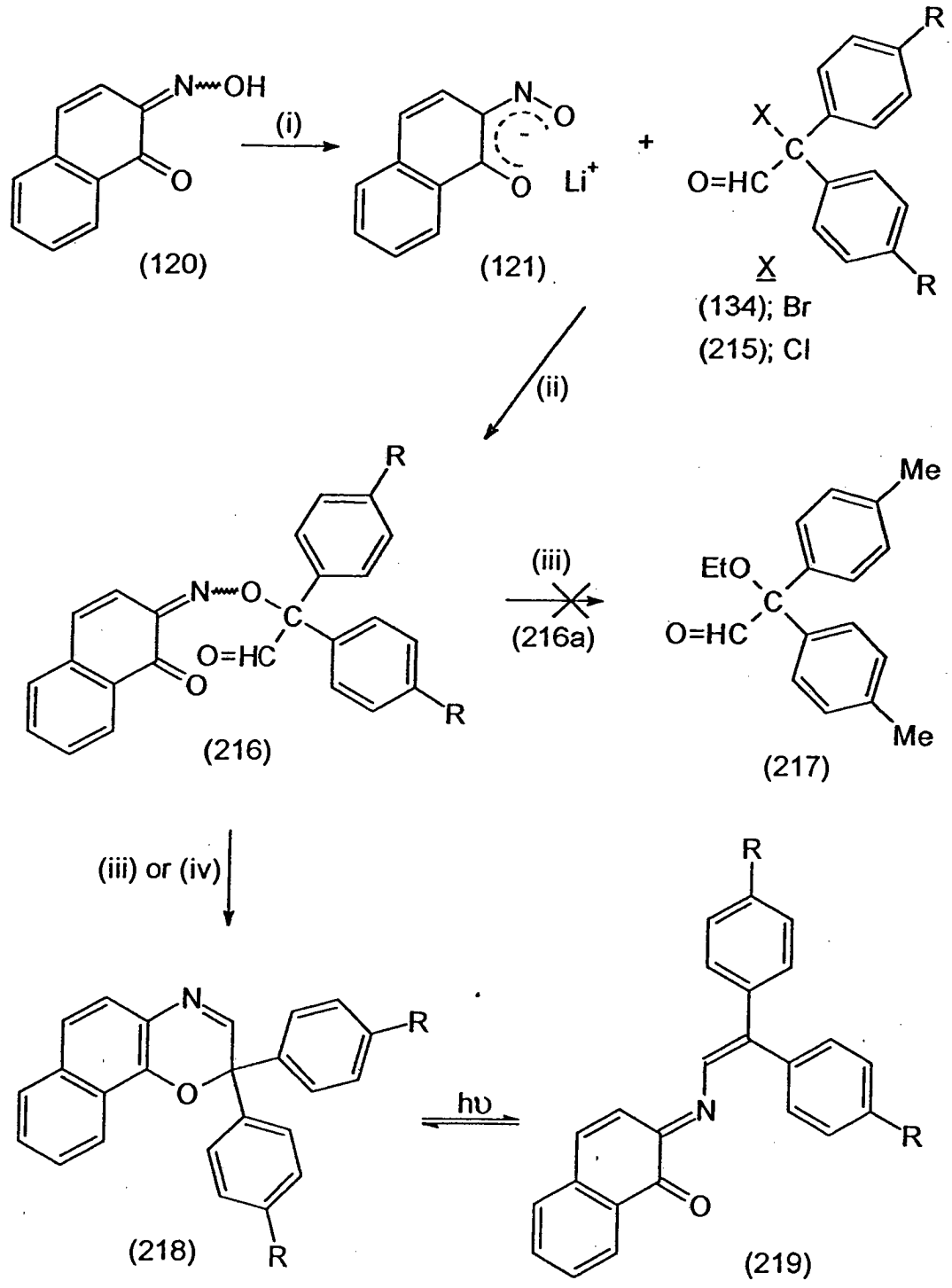
(iv) DME, room temp.

Scheme 47

aldehydic proton (δ_H 9.98) is due to the *anti* isomer. The mixture of *syn* and *anti* isomers of the oxime ether (201c) was next heated with triphenylphosphine in 1,2-dimethoxyethane giving a crude product which yielded the photochromic trimethoxynaphthoxazine derivative (202c) in excellent yield (85%).

In parallel with the foregoing syntheses of the 9-methoxynaphthoxazine derivatives (203), the synthesis (Scheme 47) of 8-methoxynaphthoxazine derivatives [eg (214)] was also attempted. Initial studies involved the monomethylation of 2,6-dihydroxynaphthalene (208) as it was expected that the known[152] 6-methoxy-2-naphthol (209) could be selectively nitrosated in the 2-position to give known[152] 6-methoxy-1,2-naphthalenedione 1-oxime (211), the lithium salt (212) of which could then be condensed with the bromo-aldehyde (199a). The resulting oxime ether (213) could then cyclise to give the desired 8-methoxynaphthoxazine derivative (214). In practice, treatment of a dimethylformamide solution of 2,6-dihydroxynaphthalene (208) with one equivalent of sodium hydride at 10°C followed by reaction with dimethyl sulphate at 100°C gave a mixture from which 6-methoxy-2-naphthol (209) was isolated in poor yield (26%). Also isolated from this reaction was a poor yield (19%) of 2,6-dimethoxynaphthalene (210). In an alternative experiment, 2,6-dihydroxynaphthalene (208) was treated at 10°C with two equivalents of sodium hydride in dimethylformamide and the resulting *bis*-anion was reacted with dimethyl sulphate at room temperature. Reaction under these conditions gave poor yields of both 6-methoxy-2-naphthol (209) (21%) and 2,6-dimethoxynaphthalene (210) (17%).

The nitrosation of 6-methoxy-2-naphthol (208) was next attempted using sodium nitrite in aqueous acetic acid at 10°C to room temperature. However, the product isolated from this reaction was an intractable brown solid which could not be purified. Commercially available 1,2-naphthalenedione 1-oxime [Scheme 24; (107)] which often requires purification by flash-chromatography prior to use can nevertheless be converted to its lithium salt (112) in excellent yield through treatment with lithium hydroxide in aqueous acetone. Having failed to purify 6-methoxy-1,2-naphthalenedione 1-oxime [Scheme 47; (211)] an attempt was made to prepare its lithium salt (212). It was hoped that the pure lithium salt (212) could be isolated and therefore separated from any contaminants in the dione oxime (211). The reaction of the presumed methoxynaphthalenedione monoxime (211) with lithium hydroxide in aqueous acetone gave a brown solid product. As previously isolated lithium salts had been used without purification, reaction of the material believed to be the lithium salt (212) with the bromo-aldehyde (199a) was investigated in an attempt to assess the effectiveness of the attempted nitrosation [(209)→(211)] and the salt formation [(211)→(212)]. Thus the crude product believed to contain the lithium salt (212) was treated with 2-bromo-2,2-diphenylacetaldehyde (199a) at room temperature in 1,2-dimethoxyethane. As only a complex gum was obtained from this reaction and none of the desired oxime ether (213) was isolated, studies on the synthesis of 8-methoxynaphthoxazine derivatives [eg (214)] were terminated at this point.



(i) LiOH, acetone, H_2O, room temp.

(ii) acetone or DME, room temp.

(iii) Ph_3P, EtOH, DME, reflux.

(iv) Ph_3P, DME, reflux.

R

a; Me

b; CF_3

c; NMe_2

d; OMe

Scheme 48

2.3 Studies on the Synthesis of 2,2-Diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazine Derivatives

During previous studies at Edinburgh,[137] two examples of photochromic naphth-1,4-oxazine derivatives were synthesised, namely 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine [see Page 25, Scheme 24; (116)] and 2,2-diphenyl-2*H*-naphth[1,2-*b*]-1,4-oxazine [see Page 26, Scheme 26; (123)]. The development of the methodology used to prepare the former has resulted in the synthesis of a number of novel 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazines [see Page 27, Scheme 29; (137)] and accounts for the majority of the work described so far in this chapter. Attention was next turned to the application of this methodology to the synthesis (Scheme 48) of further 2,2-diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazines (218) with initial efforts concentrating on the di-(4-methylphenyl) derivative (218a). The synthesis of 2*H*-naphth[1,2-*b*]-1,4-oxazines (218) is desirable as their coloration and fade kinetics are likely to differ from the 3*H*-naphth[2,1-*b*]-1,4-oxazines [Scheme 24; (116)]. Indeed, comparison of the open-chain form [Scheme 48; (219a)] of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) with the ring opened-form [Scheme 29; (138a)] of 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a) reveals that the ring-opened form (138a) of the naphth[2,1-*b*]-1,4-oxazine (137a) could be destabilised due to steric crowding between the highlighted hydrogens in the 10-position of the naphthalene ring and the 2-position of the oxazine ring. No such crowding could occur in the coloured form (219a) its reversion to the naphth[1,2-*b*]-1,4-oxazine (218a) and therefore its fade rate may be significantly slower. A comparison of identically

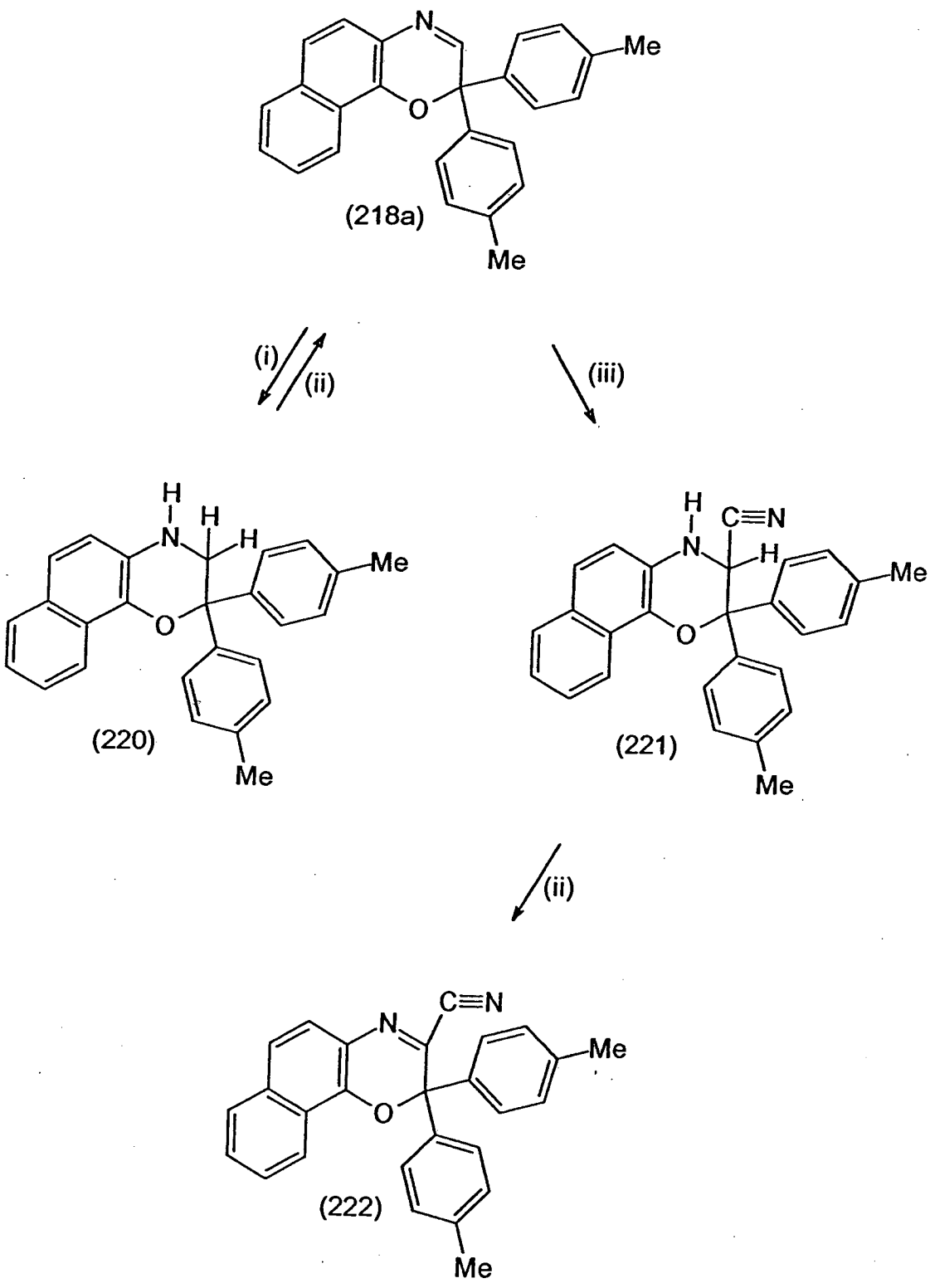
substituted 3*H*-naphtho[2,1-*b*]pyran and 2*H*-naphtho[1,2-*b*]pyran[68] shows that this change in orientation of the naphthalene nucleus causes a forty-fold decrease in fade rate.

Initial studies (Scheme 48) on the synthesis of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) involved the preparation of the 1,2-naphthalenedione 2-oxime lithium salt (121) and its condensation with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a). It was hoped that 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) would result and then cyclise on reaction with triphenylphosphine to give the naphthoxazine derivative (218a). The known[137] lithium salt (121) was previously prepared[137] (Scheme 26) in good yield (77%) through the reaction of 1,2-naphthalenedione 2-oxime (120) with lithium hydride in anhydrous 1,2-dimethoxyethane. However, in a simpler and more robust preparation, reaction (Scheme 48) of an acetone solution of 1,2-naphthalenedione 2-oxime (120) with aqueous lithium hydroxide gave the lithium salt (121) in quantitative yield.

The condensation of the lithium salt (121) with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a) proceeded smoothly at room temperature in acetone giving a moderate yield (62%) of a yellow solid product whose combustion analysis and mass, ir and ^{1}H nmr spectra are consistent with its formulation as the oxime ether (216a). Thus the ir spectrum shows two carbonyl absorption bands (ν_{max} 1732 and 1678 cm^{-1}) while the ^{1}H nmr

spectrum contains a one-proton singlet at δ_H 9.97 attributable to the aldehyde group and a six-proton singlet attributable to the two methyl groups in addition to signals due to the protons of the naphthalene nucleus and the two aryl substituents. The ^{1}H nmr spectrum of the oxime ether (216a) indicates the presence of only one compound with no *syn-anti* isomerism observed. In the absence of crystals suitable for X-ray diffraction studies, unequivocal assignment of the geometry of the oximino functionality cannot be made. However, as was proved by Rowe[137] in the case of the diphenyl analogue of (216a) [see Page 26, Scheme 26; (122)], *anti* geometry with respect to the quinone carbonyl group is most likely due to steric factors.

1,2-Naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) was next treated with triphenylphosphine in refluxing 1,2-dimethoxyethane. Reaction under these conditions gave a poor yield (41%) of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) whose structure was fully supported by its analytical and spectroscopic properties. The reaction of the oxime ether (216a) with triphenylphosphine was also performed in the presence of ethanol in an attempt to gain information on the mechanism of the formation of the naphthoxazine (218a). It was hoped that any cationic species formed during the reaction would be trapped. For example, a di-(4-methylphenyl)formylmethyl cation, a possible intermediate in this reaction, could be identified as it would be expected to react with ethanol to give the ether (217). In practice, heating the oxime ether (216a) with triphenylphosphine in 1,2-dimethoxyethane and ethanol gave only the



(i) $NaBH_4$, H_2O, DME, room temp.

(ii) MnO_2, DME, room temp.

(iii) KCN, AcOH, 100°C

Scheme 49

naphthoxazine derivative (218a) in poor yield (29%) and a series of intractable gums.

In view of the fact that the naphthoxazine derivative (218a) can be considered as a cyclic imine, it was decided to investigate its chemical behaviour in this context. Reduction (Scheme 49) of the imine functionality of the naphthoxazine derivative (218a) was expected to yield the dihydro derivative (220). Thus, treatment of the naphthoxazine derivative (218a) with sodium borohydride at room temperature in aqueous 1,2-dimethoxyethane gave a moderate yield (47%) of a product whose combustion analysis and mass and ir spectra support its formulation as the dihydro derivative (220). The ^{1}H nmr spectrum of the dihydronaphthoxazine derivative (220) displays some unusual features. While multiplets due to the tolyl substituents are observed as expected, the naphthalene nucleus gives rise to a broad singlet (δ_H 8.00-6.50). The integral of this broad signal indicates that it is also due in part to the protons of the N-H and methylene groups. This coalescence of signals is likely to be due to the ability of the reduced oxazine ring to adopt more than one conformation. Ring inversion is apparently occurring too rapidly for sharp signals due to each conformation to be detected and therefore a broad signal results On shaking with deuterium oxide, multiplets due to the protons of the naphthalene nucleus are observed and the methylene group gives rise to a sharp singlet (δ_H 3.88). It is possible that the exchange of hydrogen for deuterium at the amino functionality affects the rate of ring inversion and hence signal coalescence is not observed.

Oxidation of the dihydronaphthoxazine derivative (220) was also attempted. Treatment of an acetonitrile solution of the dihydro compound (220) with manganese dioxide at room temperature regenerated the naphthoxazine derivative (218a) though only in poor yield (33%).

The naphthoxazine (218a) derivative also behaved as expected toward the nucleophilic addition of hydrogen cyanide across the imine double bond. Thus, the naphthoxazine derivative (218a) was heated with potassium cyanide at 100°C in glacial acetic acid. Reaction under these conditions gave a moderate yield (54%) of the cyanodihydronaphthoxazine derivative (222) which analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with its assigned structure. The ir spectrum shows absorption bands attributable to the N-H group at ν_{max} 3405 and 1640 cm^{-1} though no band attributable to the cyano group is visible. The ^{1}H nmr spectrum shows a one-proton singlet δ_H 5.28 due to the methine group and a further one-proton broad singlet at δ_H 4.42 which is removed on shaking with deuterium oxide and is therefore assignable to the N-H group. Also present in the ^{1}H nmr spectrum are signals due to the aromatic protons and two three-proton singlets at δ_H 2.34 and 2.19 due to the methyl groups.

The oxidation of cyanodihydronaphthoxazine derivative (221) was next attempted to further support this structure. Treatment of (221) with manganese dioxide at room temperature in anhydrous 1,2-dimethoxyethane gave a quantitative yield of a product whose analytical and spectroscopic

properties confirm its identity as the cyanonaphthoxazine derivative (222). In this case the ir spectrum does show a cyanide absorption band (ν_{max} 2218 cm^{-1}) and the ^1H nmr spectrum shows multiplets accounting for the twenty aromatic protons.

Having further characterised the 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) work was started on the synthesis (Scheme 48) of analogous 2*H*-naphth[1,2-*b*]-1,4-oxazines (218) with a range of 4-substituted aromatic groups in the 2-position. Owing to the availability of the previously prepared 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) the synthesis of 2,2-di-(4-trifluoromethylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218b) was first attempted. Treatment of the bromo-aldehyde (134b) with the 1,2-naphthalenedione 2-oxime lithium salt (120) at room temperature in acetone gave the desired 1,2-naphthalenedione 2-oxime di-(4-trifluoromethylphenyl)-formylmethyl ether (216b) in disappointing yield (32%). Repetition of the reaction of the bromo-aldehyde (134b) with the lithium salt (120) at room temperature using 1,2-dimethoxyethane as solvent gave the oxime ether (216b) in slightly improved yield (44%).

The reaction of 1,2-naphthalenedione 2-oxime di-(4-trifluoromethylphenyl)-formylmethyl ether (216b) with triphenylphosphine was next attempted with the aim of preparing the naphthoxazine derivative (218b). The complex gum which resulted from this reaction was purified by flash-chromatography and yielded a small amount (0.6%) of a grey-green solid identified by its high

resolution mass spectrum as 2,2-di-(4-trifluoromethylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218b). Owing to the poor yield of this product, its photochromism could not be assessed.

Work was also undertaken to synthesise the analogous 2,2-di-(4-*N,N*-dimethylaminophenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218c). It was hoped that reaction of the product tentatively formulated as 2-bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (134c) with 1,2-naphthalenedione 2-oxime lithium salt (121) would give the oxime ether (216c) precursor to the naphthoxazine derivative (218c). Success in these reactions would also provide further evidence for the structure of the poorly characterised bromo-aldehyde (134c). However, reaction of the bromo-aldehyde (134c) with the lithium salt (121) at room temperature in acetone gave only a complex mixture from which only 1,2-naphthalenedione 1-oxime (120) was isolated (23%).

In contrast with the attempted preparation of 2,2-di-(4-*N,N*-dimethylaminophenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218c), studies on the synthesis of 2,2-di-(4-methoxyphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218d) were much more fruitful. Condensation of 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (215d) with 1,2-naphthalenedione 2-oxime lithium salt (121) proceeded in moderate yield (44%) at room temperature in 1,2-dimethoxyethane. The resulting 1,2-naphthalenedione 2-oxime di-(4-methoxyphenyl)formylmethyl ether (216d) gave a correct combustion analysis and mass, ir and ^{1}H nmr spectra consistent with its assigned structure. The

X-Ray Diffraction Data for 2,2-Di-(4-methoxyphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218d)

Table 5: Bond Lengths (Angstroms) with Standard Deviations

0(1)-C(10B)	1.384(3)	C(10A)-C(10B)	1.412(4)
0(1)-C(4)	1.460(4)	C(11)-C(16)	1.373(4)
C(3)-N(4)	1.281(4)	C(11)-C(12)	1.388(4)
C(3)-C(4)	1.517(4)	C(12)-C(13)	1.377(4)
C(4)-C(19)	1.509(4)	C(13)-C(14)	1.388(4)
C(4)-C(11)	1.523(4)	C(14)-0(17)	1.368(4)
C(4A)-C(10B)	1.370(4)	C(14)-C(15)	1.374(4)
C(4A)-C(5)	1.408(4)	C(15)-C(16)	1.382(4)
C(4A)-N(4)	1.409(4)	0(17)-C(18)	1.414(4)
C(5)-C(6)	1.355(5)	C(19)-C(24)	1.377(4)
C(6)-C(6A)	1.413(5)	C(19)-C(20)	1.388(4)
C(6A)-C(10A)	1.414(4)	C(20)-C(21)	1.389(4)
C(6A)-C(7)	1.417(5)	C(21)-C(22)	1.384(4)
C(7)-C(8)	1.354(5)	C(22)-0(25)	1.363(4)
C(8)-C(9)	1.404(5)	C(22)-C(23)	1.375(4)
C(9)-C(10)	1.370(4)	C(23)-C(24)	1.385(4)
C(10)-C(10A)	1.392(4)	0(25)-C(26)	1.426(4)

Table 6: Bond Angles (Degrees) with Standard Deviations

C(3)-C(4)-C(11)	109.7(3)	C(16)-C(11)-C(4)	121.8(3)
C(10B)-C(4A)-C(5)	118.6(3)	C(12)-C(11)-C(4)	120.3(3)
C(10B)-C(4A)-N(4)	121.0(3)	C(13)-C(12)-C(11)	120.5(3)
C(5)-C(4A)-N(4)	120.2(3)	C(12)-C(13)-C(14)	120.6(3)
C(3)-N(4)-C(4A)	115.8(3)	0(17)-C(14)-C(15)	124.5(3)
C(6)-C(5)-C(4A)	120.5(4)	0(17)-C(14)-C(13)	116.1(3)
C(5)-C(6)-C(6A)	121.3(3)	C(15)-C(14)-C(13)	119.4(3)
C(6)-C(6A)-C(10A)	119.4(4)	C(14)-C(15)-C(16)	119.3(3)
C(6)-C(6A)-C(7)	122.4(4)	C(11)-C(16)-C(15)	122.3(3)
C(10A)-C(6A)-C(7)	118.2(4)	C(14)-0(17)-C(18)	116.7(3)
C(8)-C(7)-C(6A)	121.3(4)	C(24)-C(19)-C(20)	117.1(3)
C(7)-C(8)-C(9)	119.8(4)	C(24)-C(19)-C(4)	120.3(3)
C(10)-C(9)-C(8)	120.5(4)	C(20)-C(19)-C(4)	122.6(3)
C(9)-C(10)-C(10A)	120.5(4)	C(19)-C(20)-C(21)	121.3(3)
C(10)-C(10A)-C(10B)	123.3(3)	C(22)-C(21)-C(20)	120.0(3)
C(10)-C(10A)-C(6A)	119.6(3)	0(25)-C(22)-C(23)	124.7(3)
C(10B)-C(10A)-C(6A)	117.0(3)	0(25)-C(22)-C(21)	115.6(3)
C(4A)-C(10B)-0(1)	119.5(3)	C(23)-C(22)-C(21)	119.6(3)
C(4A)-C(10B)-C(10A)	123.1(3)	C(22)-C(23)-C(24)	119.3(3)
0(1)-C(10B)-C(10A)	117.4(3)	C(19)-C(24)-C(23)	122.7(3)
C(16)-C(11)-C(12)	117.9(3)	C(22)-0(25)-C(26)	117.3(3)

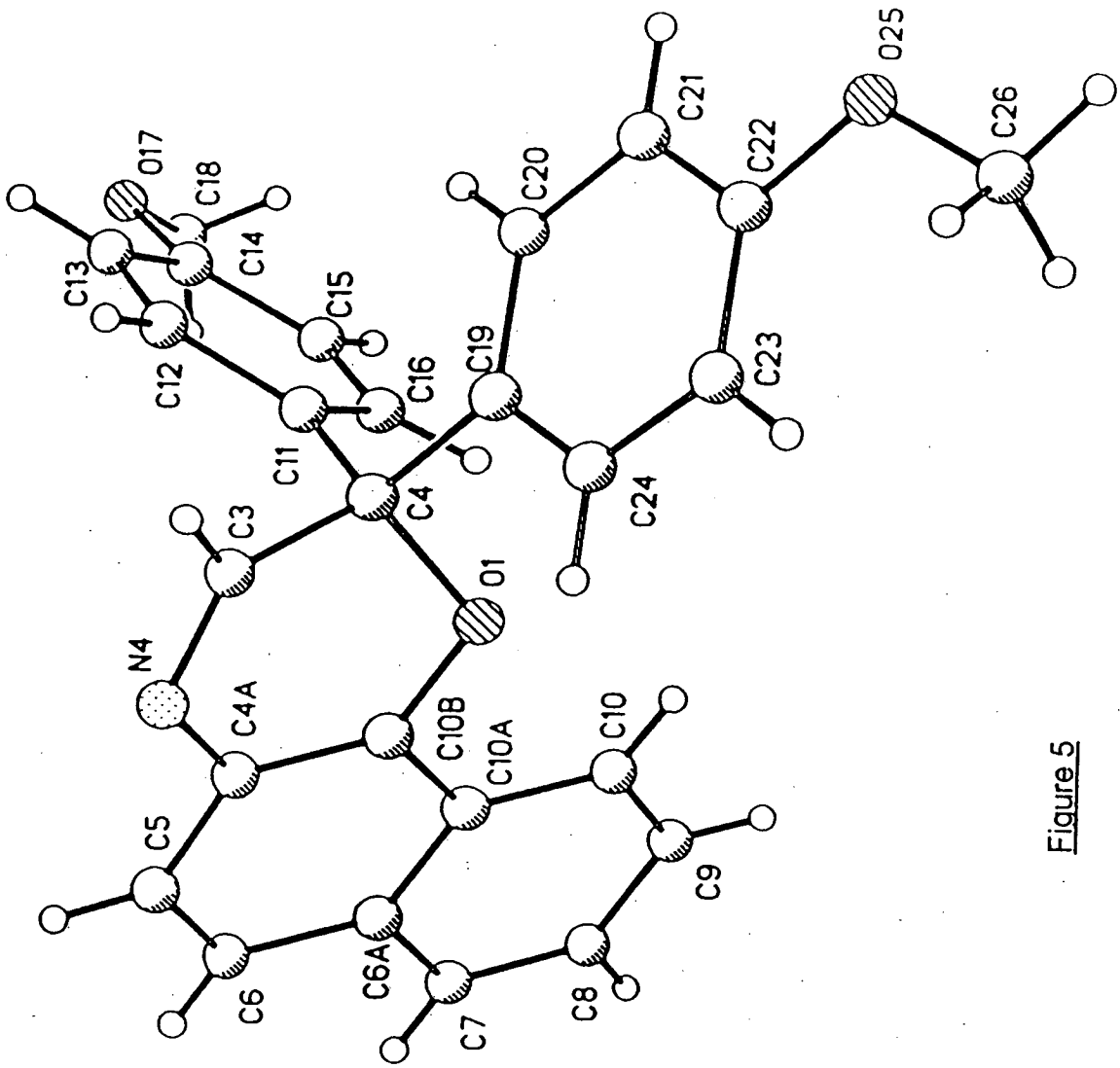
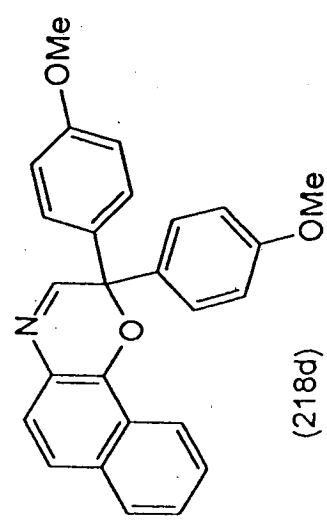
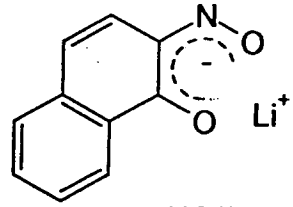


Figure 5



(218d)



(121)

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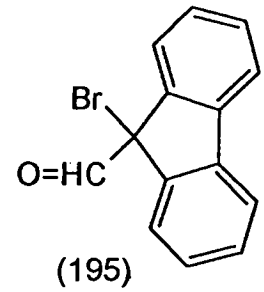
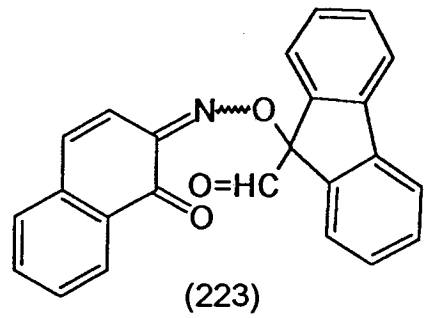


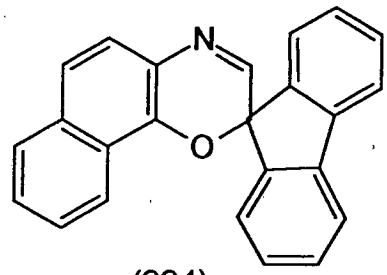
(195)

(i)



(223)

(ii)



(224)

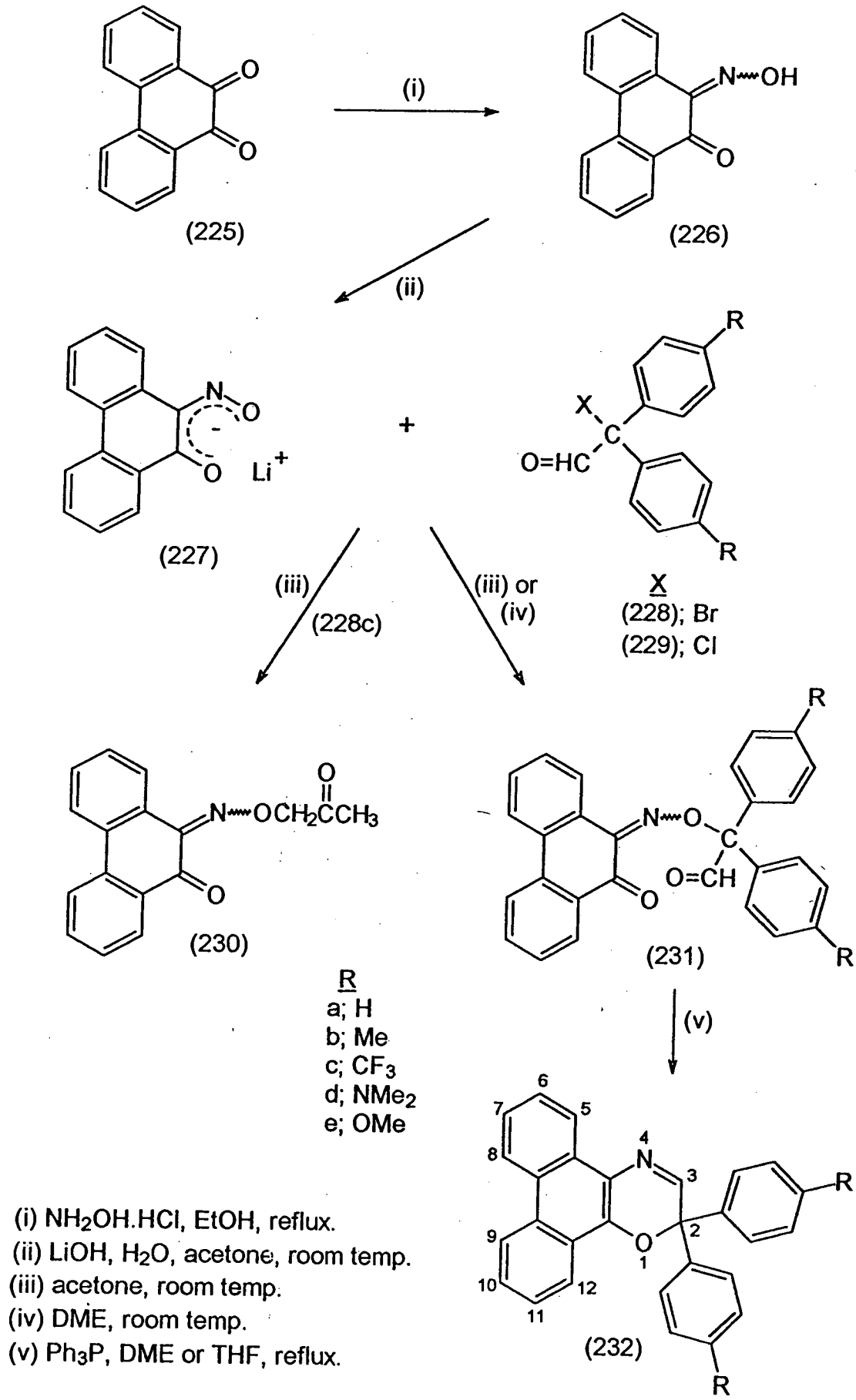
(i) acetone, room temp.

(ii) Ph_3P, THF, reflux.

Scheme 50

^{1}H nmr spectrum shows a one-proton singlet (δ_H 9.93) attributable to the aldehyde group, a six-proton singlet (δ_H 3.79) due to the methoxy groups and multiplets due to the olefinic and aromatic protons. Assignment of *syn* or *anti* geometry to the oxime ether (216d) is not possible as crystals suitable for X-ray diffraction studies could not be obtained. Conversion of the oxime ether (216d) into the naphthoxazine derivative (218d) was next attempted. Treatment of the oxime ether (216d) with triphenylphosphine in refluxing 1,2-dimethoxyethane afforded a moderate yield (52%) of a photochromic product whose analytical and spectroscopic properties are fully in accord with its formulation as the dianisylnaphthoxazine derivative (218d). Crystals of the naphthoxazine derivative (218d) were also sent for X-ray diffraction analysis, the result of which is shown in Figure 5 (see Page 81). Relevant bond lengths and bond angles are displayed in Tables 5 and 6.

In addition to the studies on the preparation of 2,2-diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazine derivatives, the synthesis (Scheme 50) of 2,2-spirofluoren-9-yl-2*H*-naphth[1,2-*b*]-1,4-oxazine (224) was also attempted. Using 9-bromofluorene-9-carboxaldehyde (195) and 1,2-naphthalenedione 2-oxime lithium salt (121) as starting materials, it was hoped that 1,2-naphthalenedione 2-oxime 9-formylfluoren-9-yl ether (223) could be prepared and then cyclised to give the desired naphthoxazine derivative (224). In practice, reaction of the lithium salt (121) with the bromo-aldehyde (195) at room temperature in acetone gave a good yield (67%) of a yellow solid product which analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with it being a single isomer of the


(i)
(ii)
(225)
(226)
(227)
(228c)
(iii)
(iii) or
(iv)
X
(228); Br
(229); Cl
(230)
(231)
(v)
(232)
R
a; H
b; Me
c; CF_3
d; NMe_2
e; OMe
(i) $NH_2OH.HCl$, EtOH, reflux.
(ii) LiOH, H_2O, acetone, room temp.
(iii) acetone, room temp.
(iv) DME, room temp.
(v) Ph_3P, DME or THF, reflux.

Scheme 51

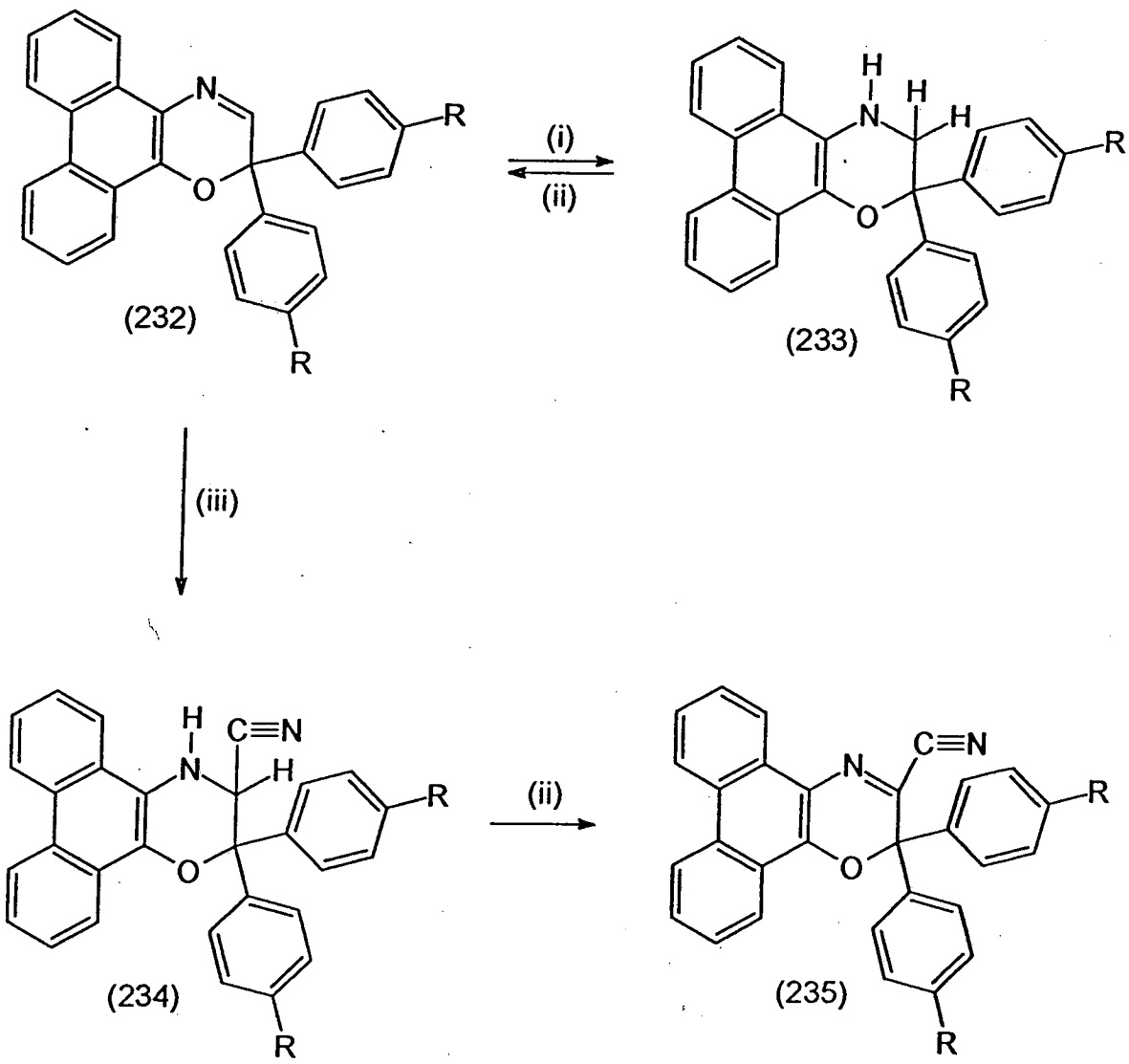
oxime ether (223). Cyclisation of the oxime ether (223) was next attempted using triphenylphosphine under reflux in 1,2-dimethoxyethane. However, reaction under these conditions gave only intractable gums. Repetition of the reaction in refluxing tetrahydrofuran gave a complex mixture of products. Tlc of the mixture revealed that one photochromic product had been formed flash-chromatography afforded a small amount of an oil whose high resolution mass spectrum indicates it to contain the desired naphthoxazine derivative (224). The uv/visible spectra of the naphthoxazine derivatives which were obtained in pure form are detailed at the end of this chapter (see Section 2.7, Page 102).

2.4 Studies on the Synthesis of 2,2-Diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine Derivatives

The aim of the work described in Chapter 2 of this thesis is the development of a structure-photochromic activity relationship for fused 2*H*-1,4-oxazine derivatives. To complement the information available from the synthesis of 3*H*-naphth[2,1-*b*]-1,4-oxazines [Scheme 23; (105)] and 2*H*-naphth[1,2-*b*]-1,4-oxazines (106), that from the synthesis (Scheme 51) of the 2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (232) is desirable. Studies under this heading initially centred on the synthesis of 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a). In this case the key starting material was the lithium salt (227) of the known[153] 9,10-phenanthrenedione 9-oxime (226). Reaction of the lithium salt (227) with 2-bromo-2,2-diphenylacetaldehyde (228a) was

expected to afford 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a). Preparation of the oxime ether (231a) would then allow its cyclisation to the phenanthro-oxazine derivative (232a)

In practice, the known[153] 9,10-phenanthrenedione 9-oxime (226) was prepared in essentially quantitative yield by the treatment of commercially available 9,10-phenanthrenedione (225) with hydroxylamine hydrochloride in refluxing ethanol. Treatment of an acetone solution of the oxime (226) with aqueous lithium hydroxide at room temperature gave a good yield (70%) of a solid product presumed to be the lithium salt (227). As with other lithium salts prepared in the course of these studies, attempts to purify and characterise (227) gave inconsistent results. The condensation of the presumed phenanthrenedione oxime lithium salt (227) and 2-bromo-2,2-diphenylacetaldehyde (228a) proceeded in excellent yield (91%) giving a yellow solid product whose analytical and spectroscopic properties support its formulation as the oxime ether (231a). Thus the ir spectrum shows absorption bands at ν_{max} 1738 and 1682 cm^{-1} due to the aldehyde and quinone carbonyl groups respectively and the ^1H nmr spectrum shows a one-proton singlet at δ_H 10.05 attributable to the aldehyde group and a series of multiplets δ_H 8.80-7.33 corresponding to the eighteen aromatic protons. No attempt was made to assign the geometry of the oximino functionality of (231a) from the spectroscopic data available.



(i) $NaBH_4$, H_2O, DME, room temp.

(ii) MnO_2, DME, room temp.

(iii) KCN, AcOH, 100°C

R
a; H
b; Me

Scheme 52

Preparation of the phenanthro-oxazine derivative (232a) was also straightforward. Treatment of the oxime ether (231a) with triphenylphosphine in refluxing 1,2-dimethoxyethane gave a poor yield (40%) of the photochromic product (232a). The phenanthro-oxazine derivative (232a) gave mass, ir and ^{1}H and ^{13}C nmr spectra consistent with its assigned structure. In the ^{1}H nmr spectrum the imine hydrogen atom appeared as a one-proton singlet at δ_H 8.09 and the aromatic protons gave a four-proton multiplet (δ_H 8.65-8.44) and a fourteen-proton multiplet (δ_H 7.71-7.23). In an attempt to improve the yield of the diphenylphenanthro-oxazine derivative (232a) the oxime ether (231a) was heated with triphenylphosphine using tetrahydrofuran as solvent. Under these conditions a poor yield (11%) of the phenanthro-oxazine derivative (232a) was isolated together with a poor recovery (18%) of the oxime ether (231a). Treatment of the oxime ether (231a) with triphenylphosphine in refluxing 1,4-dioxane also gave a yield (35%) of the phenanthro-oxazine derivative (232a) inferior to that obtained through reaction in 1,2-dimethoxyethane. The photochromic characteristics of the phenanthro-oxazine derivatives synthesised during these studies are described at the end of this chapter (see Section 2.7, Page 102).

In order to provide more evidence for the structure of the phenanthro-oxazine derivative (232a) its chemical behaviour at the imine functionality was investigated. Treatment (Scheme 52) of the phenanthro-oxazine derivative (232a) with sodium borohydride in aqueous 1,2-dimethoxyethane was expected to afford the 3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-

oxazine (233a) and did so in quantitative yield. The dihydrophenanthro-oxazine derivative (233a) analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with its assigned structure. A noteworthy feature of the ^{1}H nmr spectrum is the broad signal due to the methylene group (δ_H 4.00-3.00). Rapid inversion of the reduced oxazine ring appears to have resulted in the position of the signal due to the methylene group being inconstant and the coalescence of these peaks giving the observed broad resonance. On shaking with deuterium oxide, the signal due to the methylene group becomes considerably less broad. Exchanging hydrogen for deuterium may have slowed the rate of ring-inversion resulting in a sharper signal being observed.

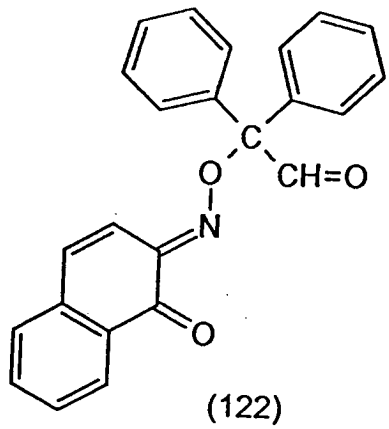
Oxidation of the dihydrophenanthro-oxazine derivative (233a) with manganese dioxide at room temperature in 1,2-dimethoxyethane regenerated the parent phenanthro-oxazine derivative (232a) in quantitative yield.

Addition of hydrogen cyanide across the imine functionality was also achieved in good yield (73%) by reaction of the phenanthro-oxazine derivative (232a) with potassium cyanide in glacial acetic acid at 100°C. The resulting 3-cyano-3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (234a) gave analytical and spectroscopic properties fully in accord with its assigned structure. Oxidation of the 3-cyano-3,4-dihydrophenanthro-oxazine derivative (234a) with manganese dioxide at room temperature in 1,2-dimethoxyethane gave a quantitative yield of a product whose analytical and spectroscopic

properties confirm its formulation as 3-cyano-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (235a).

In parallel with the synthesis of the diphenylphenanthro-oxazine derivative (232a) work was also undertaken (Scheme 51) to prepare the analogous di-(4-methylphenyl)phenanthro-oxazine derivative (232b). Using 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (228b) and the phenanthrenedione oxime lithium salt (227) as starting materials it was hoped that the target 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) could be prepared via the oxime ether (231b). In practice, condensation of the lithium salt (227) with the di-(4-methylphenyl) bromo-aldehyde (228b) at room temperature in acetone gave the oxime ether (231b) in moderate yield (45%). In turn, reaction of the oxime ether (231b) with triphenylphosphine in refluxing 1,2-dimethoxyethane gave a photochromic product (53%) which analysed correctly and gave mass, ir and ^{1}H and ^{13}C nmr spectra fully in accord with its formulation as 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b).

The preparation (Scheme 52) of the dihydro (233b) and dihydrocyano (234b) derivatives of the di-(4-methylphenyl)phenanthro-oxazine derivative (232b) was also attempted. 3,4-Dihydro-2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233b) was obtained in good yield (77%) by the reduction of (232b) with sodium borohydride at room temperature in aqueous 1,2-dimethoxyethane. The dihydro derivative (233b) analysed correctly and gave



(122)

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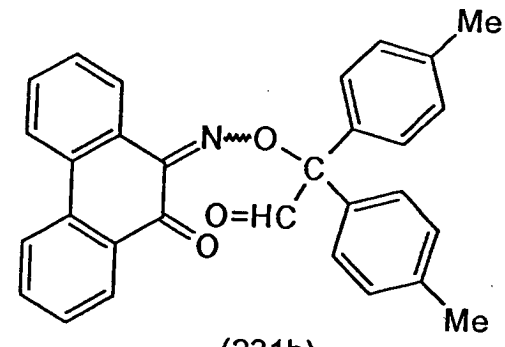
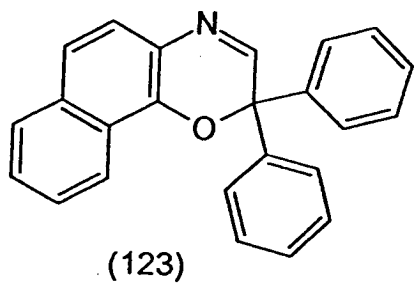


(231b)

(i)



(123)

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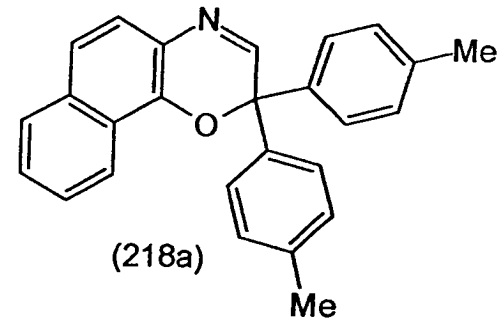

(218a)

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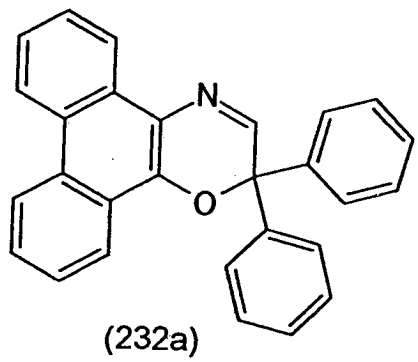
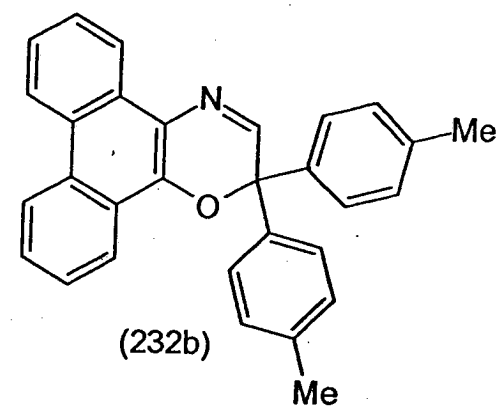


(232a)

+



(232b)

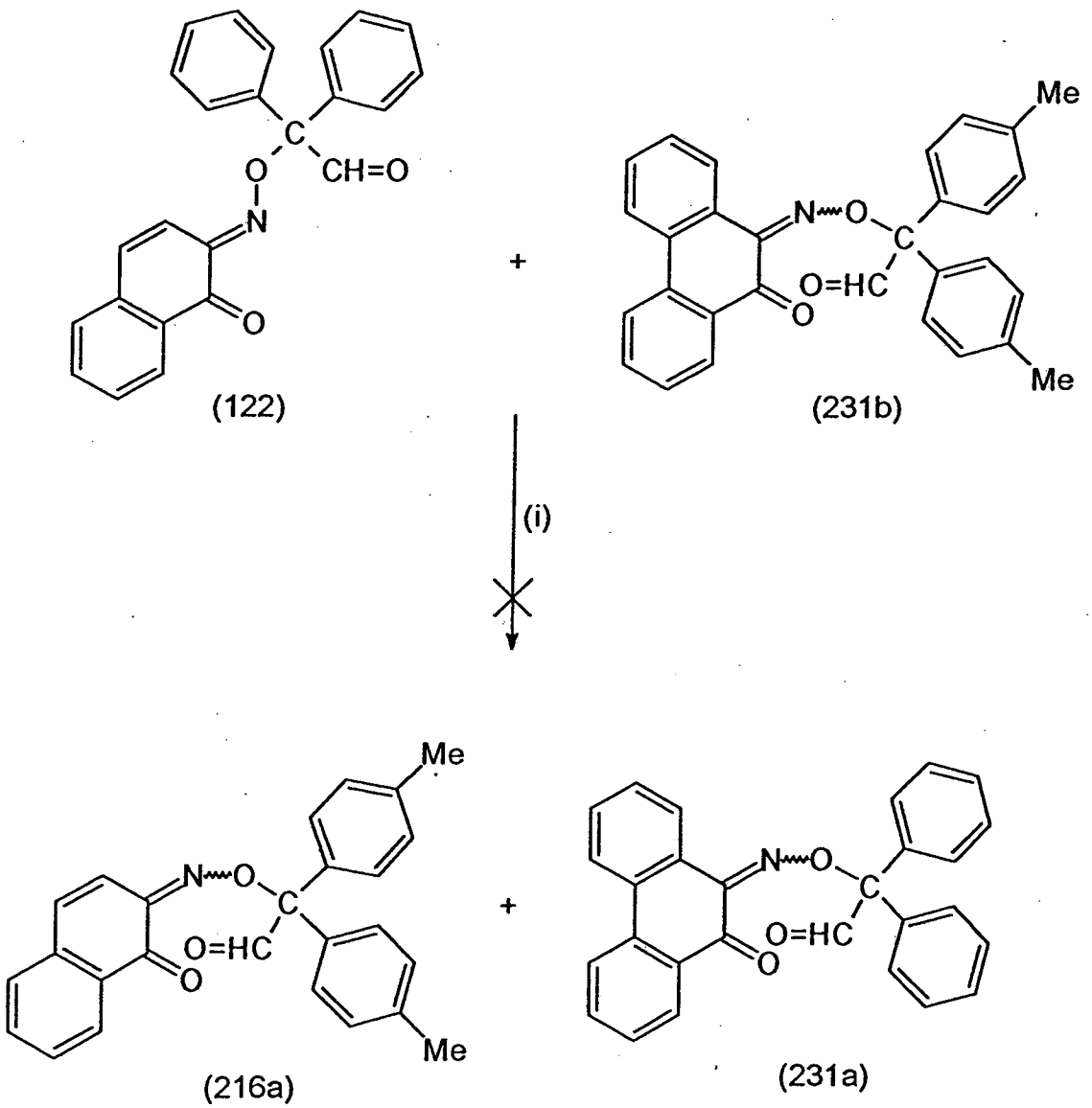
(i) Ph_3P, DME, reflux.

Scheme 53

mass, ir and ^{1}H nmr spectra consistent with its assigned structure. In turn, the dihydro derivative (233b) was found to regenerate the parent phenanthro-oxazine derivative (232b) in excellent yield (90%) on oxidation with manganese dioxide at room temperature in 1,2-dimethoxyethane. 3-Cyano-3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (234b) was next prepared in moderate yield (55%) by the treatment of the phenanthro-oxazine derivative (232b) with potassium cyanide in acetic acid at 100°C. The isolation of the dihydro (233b) and dihydrocyano (234b) derivatives provides further evidence for the structure of the phenanthro-oxazine derivative (232b).

Having furthered the synthetic methodology developed by Rowe,[137] and achieved the synthesis of several phenanthro-oxazine and naphthoxazine derivatives it was deemed appropriate at this juncture to investigate the mechanism of the formation of these novel photochromic species. During this unprecedented transformation (Scheme 51) the oxime ether precursors [eg (231)] must undergo a deep-seated rearrangement prior to or following reaction with triphenylphosphine to account for the ultimate formation of the fused 1,4-oxazine products [eg (232)]. It was desirable to establish whether the diphenylformylmethyl moiety dissociates from the rest of the molecule during this process or whether no such dissociation takes place and the process proceeds via an intramolecular rearrangement. To this end (Scheme 26) *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) was prepared to enable its reaction (Scheme 53) with triphenylphosphine in the presence of 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b)

to be studied. It was thought possible that should an intermolecular process be taking place, the reaction of a mixture of the two oxime ethers (122) and (231b) with triphenylphosphine would not only afford the expected diphenylnaphthoxazine derivative (123) and the di-(4-methylphenyl)phenanthro-oxazine derivative (232b) but also further naphthoxazine (218a) and phenanthro-oxazine (232a) derivatives. Thus (Scheme 26) the known[137] *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) was prepared in good yield (78%) by reaction of 1,2-naphthalenedione 2-oxime lithium salt (121) with 2-bromo-2,2-diphenylacetaldehyde (113) at room temperature in acetone. A sample of the oxime ether (122) was converted to the diphenylnaphthoxazine derivative (123), the only one of the possible products of this study not previously isolated. The diphenyl oxime ether (122) was then heated (Scheme 53) with 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b) and triphenylphosphine in 1,2-dimethoxyethane. While flash-chromatography failed to completely resolve the mixture of products formed, high resolution mass spectrometry shows that the diphenylnaphthoxazine (123), the di-(4-methylphenyl)naphthoxazine (128a), the diphenylphenanthro-oxazine (232a) and the di-(4-methylphenyl)phenanthro-oxazine (232b) were all formed. The formation of the 'cross-over' products (218a) and (232a) indicates that an intermolecular process must be taking place though the exact nature of the fragments involved is uncertain.



(i) DME, reflux.

Scheme 54

Having shown that the oxime ethers (122) and (231b) are cleaved at some stage during the formation of the oxazine derivatives (123), (218a), (232a) and (232b), work was undertaken (Scheme 54) to determine whether thermolysis of the oxime ethers (122) and (231b) in the absence of triphenylphosphine would lead to similar fragmentation and hence the formation of two further oxime ethers (216a) and (231a). The oxime ethers (122) and (231b) were therefore heated in 1,2-dimethoxyethane only to be recovered unchanged. Subjecting the mixture to further heating in 1,2-dimethoxyethane led only to the decomposition of the starting materials. The mass spectrum of the resulting complex mixture provided no evidence for the formation of the oxime ethers (216a) and (231a) or any other identifiable fragments of the starting materials (122) and (231b).

Having temporarily halted work on the preparation of photochromic phenanthro-oxazine derivatives, attention was once again re-focused (Scheme 51) on such syntheses and in particular on the synthesis of 2,2-di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232c). Thus the reaction of 9,10-phenanthrenedione 9-oxime lithium salt (227) with 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde at room temperature in acetone was investigated. Reaction under these conditions gave a mixture of products from which the desired 9,10-phenanthrenedione 9-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (231c) was isolated in moderate yield (40%). Also isolated were 9,10-phenanthrenedione 9-oxime (226) (37%) and a poor yield (30%) of a product whose analytical and spectroscopic properties

supports its formulation as 9,10-phenanthrenedione 9-oxime 2-oxopropyl ether (230). The ir spectrum of the oxopropyl oxime ether (230) shows carbonyl absorption bands at ν_{max} 1723 and 1670 cm^{-1} and the ^1H nmr spectrum shows, in addition to signals due to the aromatic protons, a two-proton singlet (δ_H 5.05) attributable to the methylene group and a three-proton singlet (δ_H 2.19) due to the methyl group. While the formation of the oxopropyl oxime ether (230) is surprising, it was thought possible that it may be due to the initial bromination of the acetone solvent by the bromo-aldehyde (228c) followed by reaction of the resulting bromoacetone with the lithium salt (227). In order to support this theory, the lithium salt (227) was treated with commercially available bromoacetone at room temperature in acetone. However, reaction under these conditions gave none of the 9,10-phenanthrenedione 9-oxime 2-oxopropyl ether (230) giving instead moderate yields of the unreacted lithium salt (227) (45%), the phenanthrenedione oxime (226) (54%) and an intractable gum.

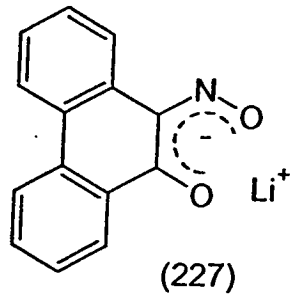
In the time available, further investigations of possible mechanisms for the formation of the oxopropyl oxime ether (230) were considered to be of less interest than optimisation of the synthesis of the di-(4-trifluoromethylphenyl)formylmethyl oxime ether (231c) and its cyclisation to the potentially photochromic 2,2-di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (231c). Thus, the condensation of the lithium salt with the bromo-aldehyde (228c) at room temperature in 1,2-dimethoxyethane gave an improved yield (63%) of the oxime ether (231c). The oxime ether (231c) was

then heated with triphenylphosphine in 1,2-dimethoxyethane. Reaction under these conditions gave a number of intractable oils, together with a disappointing yield (5%) of a product whose analytical and spectroscopic properties support its formulation as the di-(4-trifluoromethylphenyl)-phenanthro-oxazine derivative (232c).

Attempts were also made to condense the 9,10-phenanthrenedione 9-oxime lithium salt (227) with 2-bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)-acetaldehyde (228d). It was hoped that the oxime ether (231d) could be obtained as a precursor to 2,2-di-(4-*N,N*–dimethylaminophenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232d). In practice, on treatment of the lithium salt (227) with the bromo-aldehyde (228d) at room temperature in acetone, no reaction occurred and the lithium salt (227) was recovered unchanged in high yield (92%). Repetition of the attempted condensation in refluxing acetone also gave a high recovery (89%) of unreacted lithium salt (227). The lack of reactivity of the 2-bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (228d) toward the lithium salt (227) may be due to electron-donation by the dimethylamino moieties rendering the carbon-bromine bond inert to nucleophilic attack. Alternative strategies for the synthesis of the di-(4-*N,N*-dimethylaminophenyl)phenanthro-oxazine derivative (232d) are discussed later in this chapter (see Page 95, Scheme 56).

In contrast with the foregoing unsuccessful studies, the synthesis of 2,2-di-(4-methoxyphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232e) was

straightforward. Condensation of 2-chloro-2,2-di-(4-methoxyphenyl)-acetaldehyde (229e) with 9,10-phenanthrenedione 9-oxime lithium salt (227) was performed at room temperature in 1,2-dimethoxyethane. Reaction under these conditions gave unreacted lithium salt (227) (26%) and two crops of product. The major crop of product, isolated in moderate yield (38%) gave a combustion analysis and mass, ir and ^{1}H nmr spectra consistent with its formulation as the 9,10-phenanthrenedione 9-oxime di-(4-methoxyphenyl)formylmethyl ether (231e). Thus the ir spectrum shows the expected carbonyl absorption bands at ν_{max} 1739 and 1677 cm^{-1} and the ^{1}H nmr spectrum shows, in addition to the signals due to the aromatic protons, a one-proton singlet (δ_H 9.96) attributable to the aldehyde group and a six-proton singlet (δ_H 3.79) due to the methoxy groups. The minor crop of product, isolated in poor yield (9%) also analysed as the oxime ether (231e). However, its ^{1}H nmr spectrum reveals the presence not only of the product previously isolated in the major crop, but also further signals due to aromatic protons and a singlet (δ_H 9.91) attributable to a second aldehyde group. Though geometric isomerism was not observed in phenanthrenedione oxime ethers reported so far in this chapter, these features of the ^{1}H nmr spectrum of the dianisyl compound (231e) suggest that it exists as *syn* and *anti* isomers. Assignment of the geometry of the oxime linkage can only be made by comparison with the ^{1}H nmr spectra of the previously isolated *syn* and *anti* isomers of 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [see Page 26, Scheme 25; (117) and (118)] and the dianisyl derivative [see Page 53, Scheme 39; (171)] both of which gave signals due to the aldehydic protons of their *anti*



(227)

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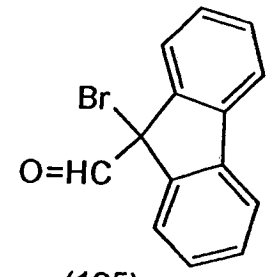
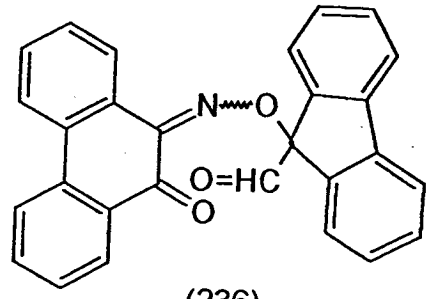


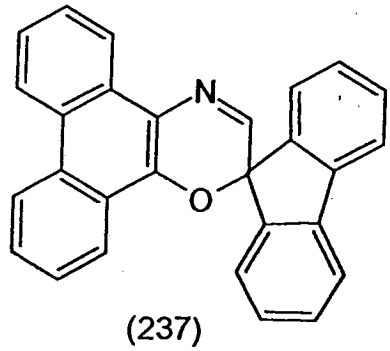
(195)

(i)



(236)

(ii)



(237)

(i) acetone, room temp.

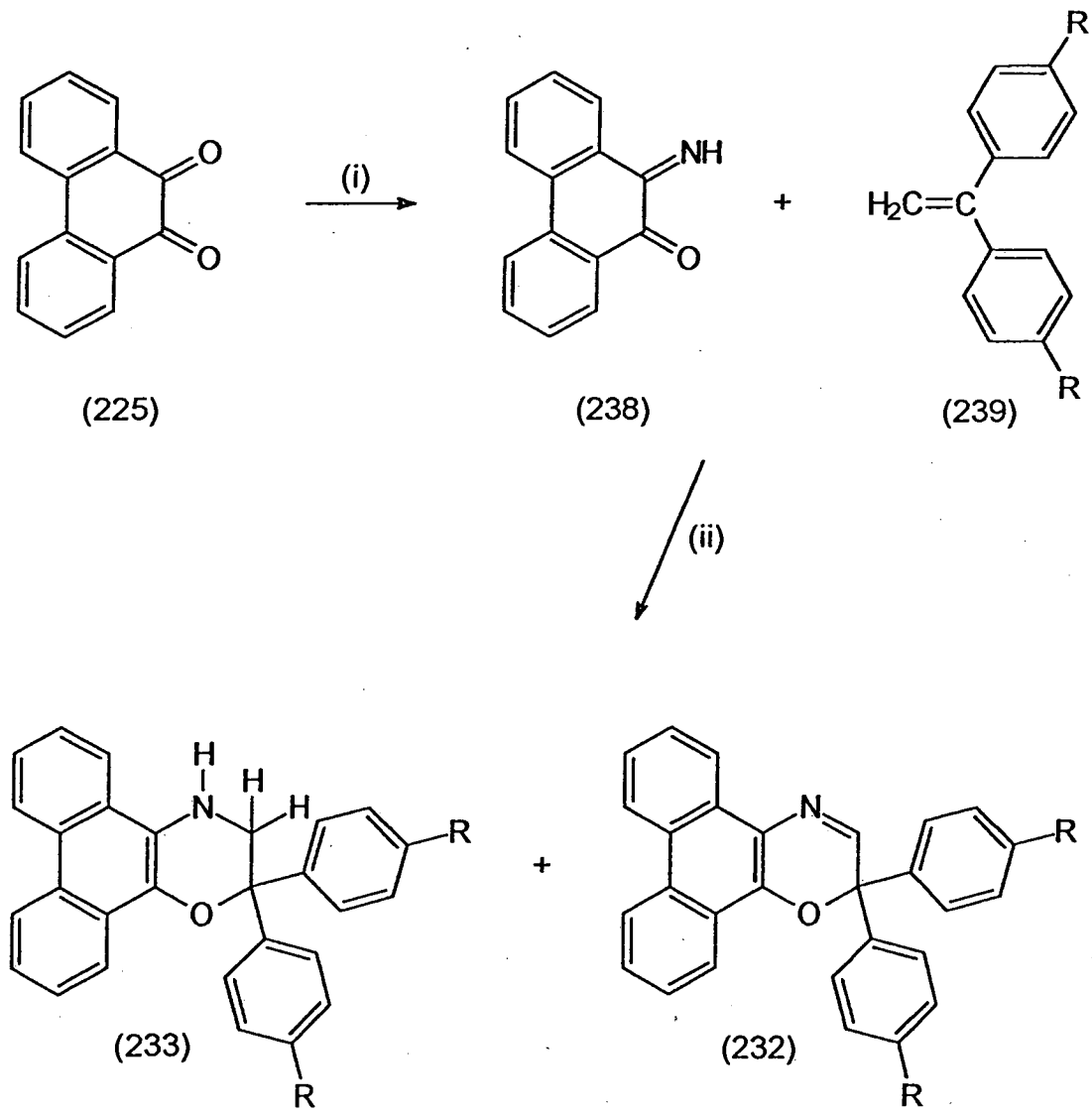
(ii) Ph_3P, DME, reflux.

Scheme 55

isomer at higher frequency than those due to the *syn* isomers. The major crop of 9,10-phenanthrenedione 9-oxime di-(4-methoxyphenyl)formylmethyl ether (231e) is assigned by this obviously imperfect comparison as the *anti* isomer and the minor crop as a 4:1 mixture of *syn* and *anti* isomers.

Treatment of the product formulated as the *anti* isomer of (231e) with triphenylphosphine in refluxing 1,2-dimethoxyethane gave a good yield (70%) of a photochromic product whose analytical and spectroscopic properties support its formulation as 2,2-di-(4-methoxyphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232e).

The potentially photochromic (Scheme 55) 2,2-spirofluoren-9-yl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (237) was also considered to be a compound worthy of investigation. With 9-bromofluorene-9-carboxaldehyde (195) available, its condensation with the lithium salt (227) was investigated. It was hoped that 9,10-phenanthrenedione 9-oxime 9-formylfluoren-9-yl ether (236) would result and that its cyclisation to the phenanthro-oxazine derivative (237) could then be induced. In practice, the oxime ether (236) was available in excellent yield (82%) by reaction of the lithium salt (227) and the bromo-aldehyde (195) in acetone at room temperature. The resulting oxime ether (236) analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with this formulation. The ir spectrum contains two carbonyl absorption bands at ν_{max} 1733 and 1676 cm^{-1} while the ^{1}H nmr spectrum shows a 10:1 mixture of two isomers with signals due to the aldehyde functionalities (δ_H 9.88 and 9.71)



(i) $NH_3(g)$, EtOH, CH_2Cl_2, reflux.

(ii) dioxane, reflux.

R

a; H

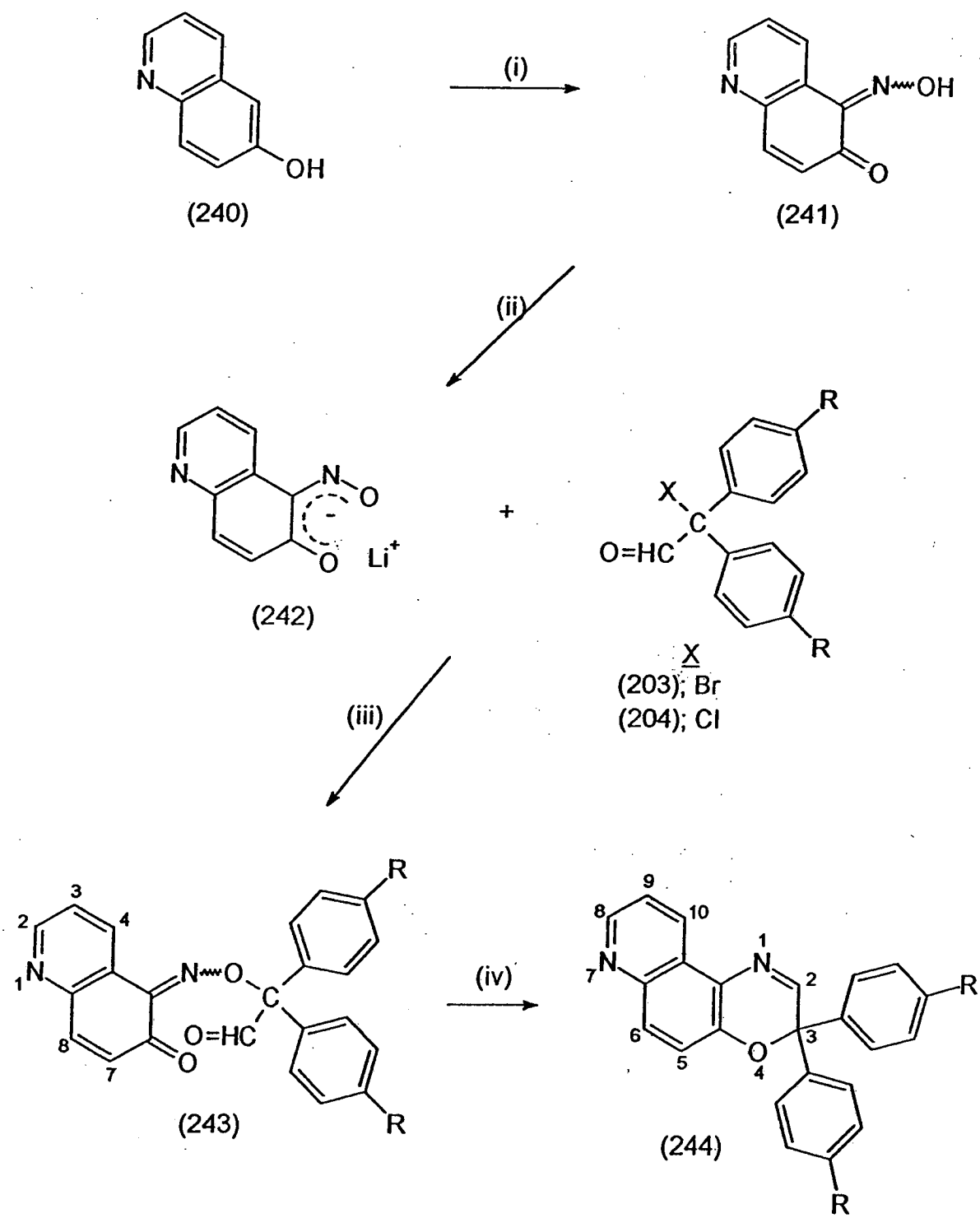
d; NMe_2

Scheme 56

and a series of multiplets due to the aromatic protons (δ_H 8.62-7.27). As in the case of the di-(4-methoxyphenyl)formylmethyl oxime ether [Scheme 51; (231e)] the assignment of *syn* or *anti* geometry to the two isomers of the fluorenyl oxime ether (236) is based only on the assumption that the signal due to the aldehyde group of the *anti* isomer will occur at higher frequency than that of the *syn* isomer. If this is indeed the case, then the fluorenyl oxime ether (236) was obtained in this reaction as a 10:1 mixture of *syn* and *anti* isomers.

The cyclisation of the oxime ether (236) was next attempted. However, reaction with triphenylphosphine in refluxing 1,2-dimethoxyethane gave none of the desired phenanthro-oxazine derivative (237) giving instead a complex gum from which no identifiable product was obtained.

As the foregoing methodology failed to give access to certain desirable phenanthro-oxazine derivatives, for example the di-(4-*N,N*-dimethylamino-phenyl) derivative [see Page 92, Scheme 51; (232d)], work was started on the development (Scheme 56) of an alternative strategy for their preparation. In a model study, the synthesis of the 3,4-dihydro derivative (233) of the 2,2-diphenylphenanthro-oxazine (232) was attempted through the preparation of the known[154] 9,10-phenanthrenedione 9-imine (238) and its reaction with commercially available 1,1-diphenylethene (239a). Thus, the imine (238) was prepared by the treatment of 9,10-phenanthrenedione (225) with gaseous ammonia in a refluxing mixture of dichloromethane and ethanol. Under these conditions, the imine (238) was isolated in excellent yield (92%). The imine



(i) $NaNO_2$, AcOH, H_2O, 10°C
(ii) LiOH, H_2O, acetone, room temp.
(iii) DME, room temp.
(iv) Ph_3P, DME, reflux.

R
a; H
b; Me
c; OMe

Scheme 57

(238) was next reacted with 1,1-diphenylethene (239a) in refluxing 1,4-dioxane. Reaction under these conditions gave a high yield (94%) of unreacted 1,1-diphenylethene (239a) and a small amount of a complex gum whose tlc indicated the presence of the dihydro compound (233a) and the photochromic phenanthro-oxazine derivative (232a) though neither were obtained in pure form. In a similar experiment, a 1,4-dioxane solution of the phenanthrenedione imine (238) was heated with Michler's alkene, 1,1-di-(4-*N,N*-dimethylaminophenyl)ethene (239d) with the aim of preparing the 3,4-dihydro-2,2-di-(4-*N,N*-dimethylaminophenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233d). Reaction under these conditions gave only a poor yield (10%) of the desired dihydrophenanthro-oxazine derivative (233d). Due to lack of time, studies on the optimisation of the forgoing syntheses were terminated at this point.

2.5 Studies on the Synthesis of 3,3-Diaryl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine Derivatives (244)

In addition to the synthesis of novel photochromic compounds consisting of disubstituted 2*H*-1,4-oxazine nuclei fused to naphthalene and phenanthrene rings, work was undertaken (Scheme 57) to synthesise further potentially photochromic fused oxazines containing other nuclei namely 3*H*-pyrido[3,2-*f*]-1,4-benzoxazines (244). Initial studies under this heading centred on the preparation of the known[155] 5,6-quinolinedione 5-oxime (241) which, it was

hoped could be converted to the lithium salt (242) then reacted with 2-bromo-2,2-diphenylacetaldehyde (203a) to give the oxime ether (243a), a potential precursor to the desired diphenylpyridobenzoxazine (244a).

The quinolinedione oxime (241) was prepared[155] in excellent yield (87%) by the reaction of commercially available 6-hydroxyquinoline (240) with sodium nitrite in aqueous acetic acid at 10°C to room temperature. In turn, treatment of the quinolinedione oxime (241) with lithium hydroxide in aqueous acetone gave a good yield (68%) of the lithium salt (242). The lithium salt (242) was next reacted with bromodiphenylacetaldehyde (203a) at room temperature in 1,2-dimethoxyethane to give a good yield (78%) of 5,6-quinolinedione 5-oxime diphenylformylmethyl ether (243a). The oxime ether (243a) analysed correctly and gave mass, ir and ^{1}H nmr spectra consistent with its assigned structure. Thus the ir spectrum shows the expected carbonyl absorption bands at ν_{max} 1726 and 1678 cm^{-1} while the ^{1}H nmr spectrum shows a one-proton singlet at δ_H 10.03 due to the aldehyde group. Also present in the ^{1}H nmr spectrum are signals due to the two phenyl rings and the quinoline nucleus. Of particular interest are the one-proton doublets due to the two olefinic protons H_8 and H_7 (δ_H 7.58 and 6.57 respectively), the former also being coupled to the *peri* proton H_4 which itself gives rise to a double double doublet (δ_H 9.16). While the oxime ether (243a) was apparently isolated as a single isomer the geometry of the oxime linkage could not be assigned.

The reaction of the oxime ether (243a) with triphenylphosphine was next attempted. Treatment of the oxime ether (243a) with triphenylphosphine in refluxing 1,2-dimethoxyethane gave a poor yield (25%) of the photochromic pyridobenzoxazine derivative (244a).

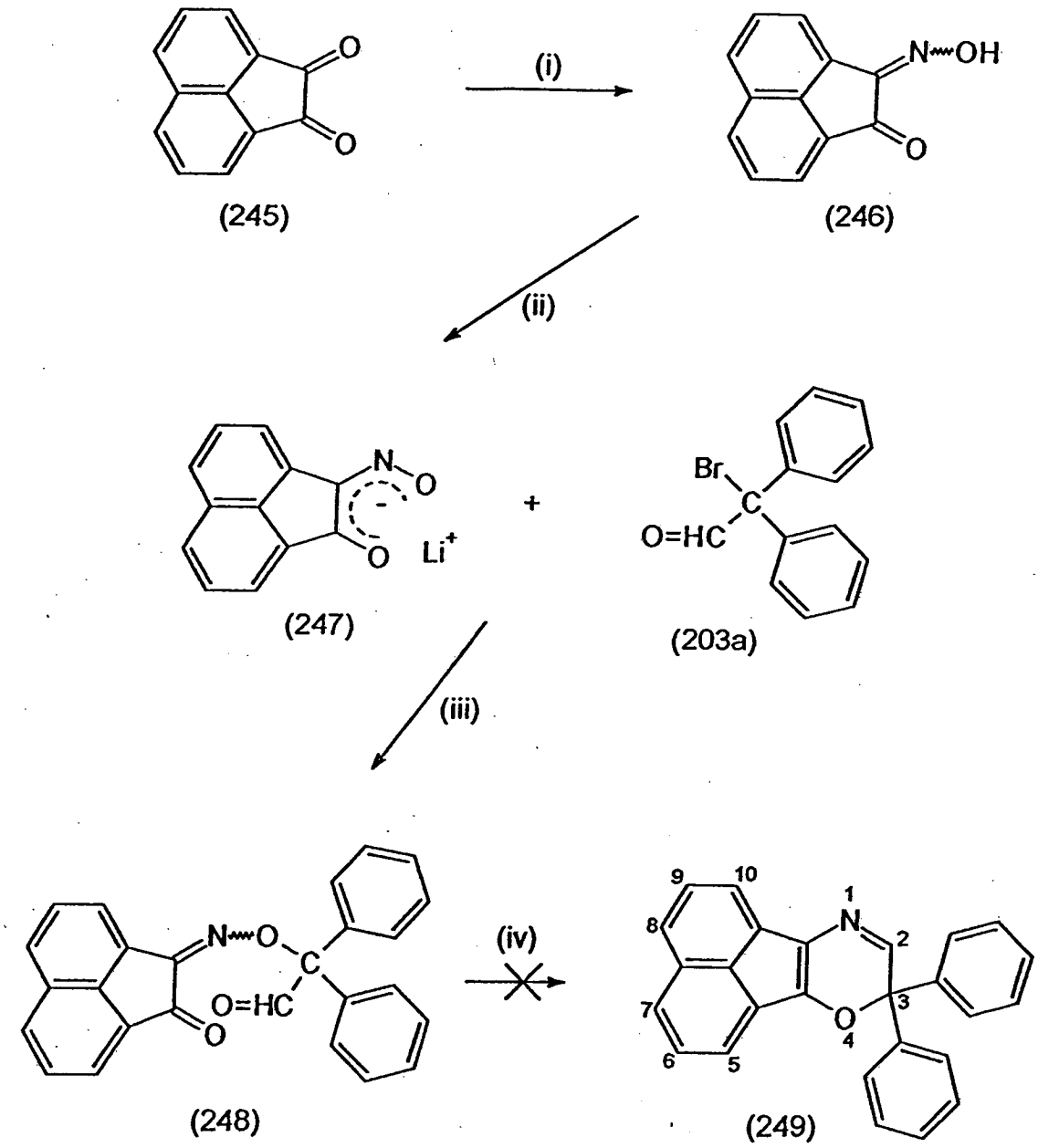
In addition to the synthesis of the diphenyl compound (244a) the di-(4-methylphenyl)pyridobenzoxazine derivative (243b) was prepared using the 5,6-quinolinedione 5-oxime lithium salt (242) and 2-bromo-2,2-(4-methylphenyl)acetaldehyde (203b) as starting materials. Reaction of the lithium salt (242) and the bromo-aldehyde (203b) at room temperature in 1,2-dimethoxyethane gave a moderate recovery (40%) of the unreacted lithium salt (242) and two crops of the oxime ether (243b). The major crop of the product, isolated in poor yield (30%) as a yellow solid, gave a combustion analysis and mass, ir and ^{1}H nmr spectra consistent with its formulation as 5,6-quinolinedione 5-oxime di-(4-methylphenyl)formylmethyl ether (243b). The ir spectrum showed the expected carbonyl absorption bands at ν_{max} 1731 and 1671 cm^{-1} The ^{1}H nmr spectrum shows signals due to the protons of the tolyl substituents and quinoline rings and singlets at δ_H 9.99 and 2.35 due to the aldehyde functionality and the methyl groups respectively. As was observed in the case of the diphenyl oxime ether (243a) the olefinic protons H_7 and H_8 give rise to two doublets (δ_H 6.54 and 7.56; J 10.2 Hz) with the latter being further coupled (J 0.6 Hz) with the *peri* proton H_4, while the *peri* proton itself appears as a double double doublet at δ_H 9.17.

The minor crop of product, isolated in very low yield (4%) as an orange solid also gave a combustion analysis correct for the oxime ether (243b). The mass spectrum of the second crop of (243b) supports its assigned structure as do the carbonyl absorption bands (ν_{max} 1726 and 1651 cm^{-1}) in its ir spectrum. However, the ^1H nmr spectrum of this second crop of the oxime ether (243b) is markedly different to that of the major crop. The one-proton singlet due to the aldehyde functionality appears at δ_H 9.90 and while the *peri* proton H_4 gives rise to the expected double double doublet, the signal appears at δ_H 8.11, a 1 ppm shift with respect to the major form. In the ^1H nmr spectra of the naphthalenedione oxime ethers [see Page 26, Scheme 25; (117) and (118)] the aldehydic protons of the *anti* isomer gave rise to a higher frequency signal than that due to the *syn* isomer. Comparison with naphthalenedione oxime ethers suggests that the major crop of the quinolinedione oxime ether (243b) is the *anti* isomer though definite assignment of the geometry of the oxime linkage is not possible. Furthermore, no explanation can be given for the dramatic difference between the chemical shifts of the signals due to the peri protons (H_4) of each species.

Reaction of the oxime ether (243b) with triphenylphosphine under reflux in 1,2-dimethoxyethane gave a moderate yield (41%) of the photochromic di-(4-methylphenyl)pyridobenzoxazine (244b) whose analytical and mass, ir and ^1H nmr spectroscopic properties support its assigned structure.

Work was also undertaken to prepare the 5,6-quinolinedione 5-oxime di-(4-methoxyphenyl)formylmethyl ether (243c) and the potentially photochromic 3,3-di-(4-methoxyphenyl)-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine (244c). The quinolinedione oxime lithium salt (242) reacted smoothly with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (204c) at room temperature in 1,2-dimethoxyethane. In addition to a poor yield (37%) of the desired oxime ether (243c), the unreacted lithium salt (242) was also obtained (38%) from this reaction. The oxime ether (243c) analysed correctly and gave mass ir and ^{1}H nmr spectra consistent with its assigned structure. The ^{1}H nmr spectrum reveals that the oxime ether (243c) was isolated as a mixture of isomers. Thus two singlets (δ_H 9.94 and 9.86) attributable to aldehydic protons were observed in an ratio of 2:5 and two double double doublets due to the *peri* protons (H_4) were also present (δ_H 9.15 and 8.12). As was observed for the *syn* and *anti* isomers of 5,6-quinolinedione 5-oxime di-(4-methylphenyl)formylmethyl ether (243b) there is a remarkable difference between the chemical shifts of the signals due to the H_4 protons of the two isomers. Assignment can only be based on the previously mentioned observation[137] that the signal due to the aldehydic proton of the *anti* isomer of 1,2-naphthalenedione 1-oxime diphenylformylmethyl ether [Scheme 25; (118)] appears at higher frequency than that of the *syn* isomer (117). By this analogy the mixture of oxime ether isomers has composition 5 *syn* : 2 *anti*

Reaction of the mixture of isomers of the oxime ether (243c) with triphenylphosphine under reflux in 1,2-dimethoxyethane afforded a good yield



(i) $NH_2OH.HCl$, EtOH, reflux.
(ii) LiOH, acetone, H_2O, room temp.
(iii) DME, room temp.
(iv) Ph_3P, DME or dioxane, reflux.

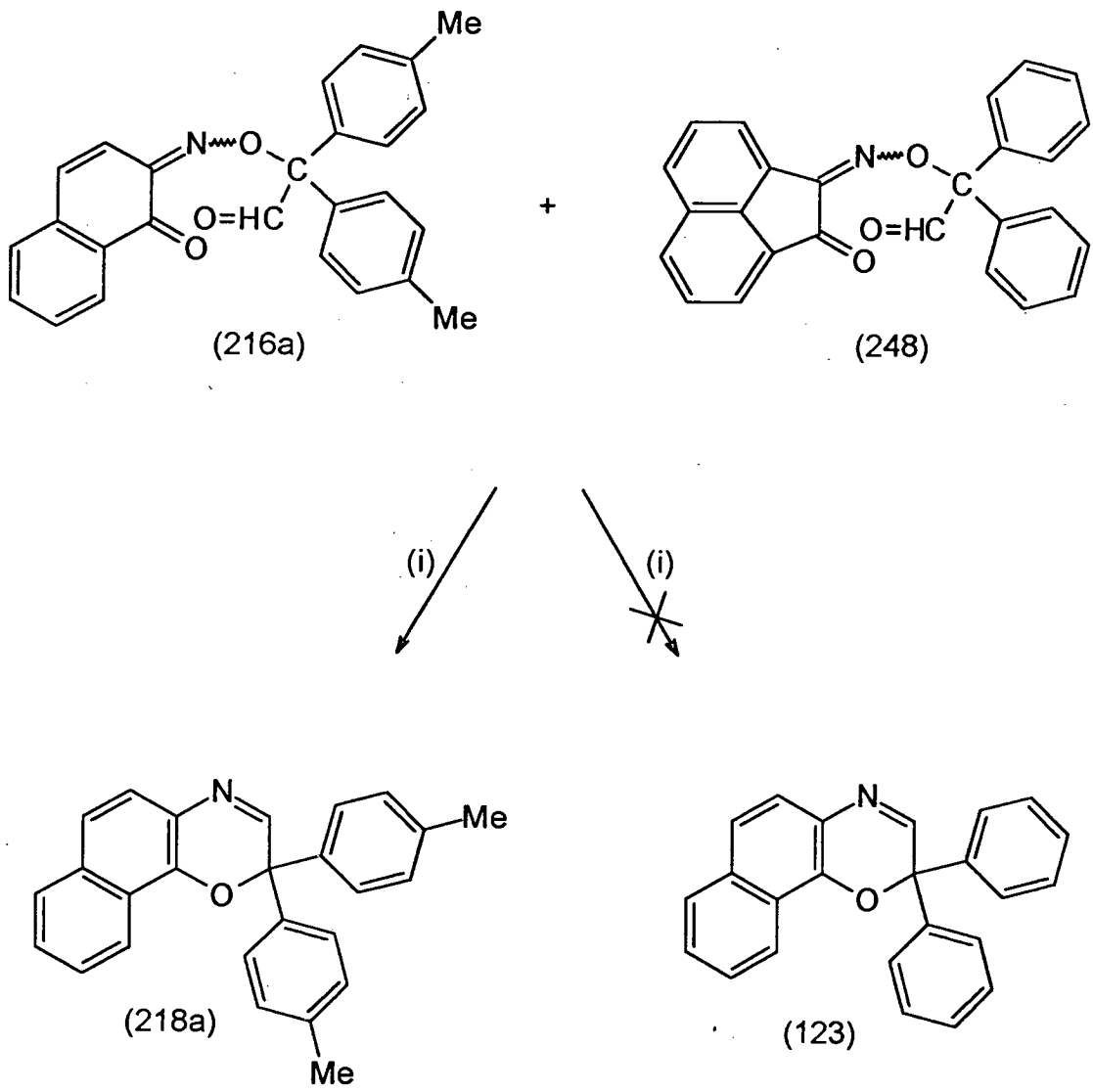
Scheme 58

(76%) of a photochromic product whose analytical and spectroscopic properties are fully in accord with its formulation as the pyridobenzoxazine (244c). The uv/visible spectra of the aforementioned pyridobenzoxazine derivatives are discussed in detail at the end of this chapter (see Section 2.7, Page 104).

2.6 Studies on the Synthesis of 2,2-Diaryl-2*H*-acenaphtho[1,2-*b*]-1,4-oxazine derivatives

In accordance with the synthetic strategy now well established, initial work under this heading concentrated on the synthesis (Scheme 58) of the 1,2-acenaphthylenedione 1-oxime lithium salt (247) and its condensation with bromodiphenylacetaldehyde (203a). It was hoped that the oxime ether (248) could be so obtained then cyclised by reaction with triphenylphosphine to give the previously undescribed acenaphtho-1,4-oxazine derivative (249).

The known[156] 1,2-acenaphthylenedione 1-oxime (246) was prepared in quantitative yield by reaction of the commercially available dione (245) with hydroxylamine hydrochloride in refluxing ethanol. Treatment of the oxime (246) with lithium hydroxide in aqueous acetone gave a high melting yellow solid presumed to be the lithium salt (247). As with the other oxime lithium salts reported in this thesis, purification of (247) was not possible and attempts to characterise it gave inconsistent results.



(i) Ph_3P, DME, reflux.

Scheme 59

The material presumed to be the lithium salt (247) reacted efficiently with 2-bromo-2,2-diphenylacetaldehyde (203a) giving a good yield (82%) of a product whose analytical and spectroscopic properties confirm its formulation as 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248). Thus the ir spectrum shows an absorption band at ν_{max} 2729 cm^{-1} due to the aldehyde functionality and a carbonyl absorption band at ν_{max} 1734 cm^{-1} presumed to be due to coincident quinone and aldehyde carbonyl groups. The ^1H nmr spectrum shows in addition to the aromatic protons, a one-proton singlet (δ_H 10.18) due to the aldehyde hydrogen. With the oxime ether (248) available, its reaction with triphenylphosphine was attempted in refluxing 1,2-dimethoxyethane. Under these conditions the desired acenaphtho-oxazine (249) was not formed and unreacted (248) was recovered in high yield (77%). Repetition of the attempted reaction in the higher boiling solvent 1,4-dioxane also gave only unreacted starting material (248) in 77% yield.

The failure of the 1,2-acenaphthylenedione oxime ether (248) to react with triphenylphosphine to give the acenaphtho-oxazine derivative (249) was disappointing and studies were initiated to investigate this negative result. In a previous study (see Page 88, Scheme 53) it was established that during the formation of fused 2*H*-1,4-oxazine derivatives [eg (123)], their oxime ether precursors [eg (122)] are cleaved into two fragments. An experiment was devised (Scheme 59) to establish whether the acenaphthylenedione oxime ether (248) possesses a resistance to cleavage of its diphenylformylmethyl moiety from the acenaphthylene nucleus. Thus a mixture of the

acenaphthylenedione oxime ether (248) and 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) was heated with triphenylphosphine in 1,2-dimethoxyethane. Though it was not expected that the acenaphtho-oxazine derivative [Scheme 58; (249)] would be isolated, the formation of the diphenylnaphthoxazine derivative (123) as well as the di-(4-methylphenyl)naphthoxazine derivative (218a) would indicate that cleavage of the acenaphthylenedione oxime ether (248) was taking place under the reaction conditions. Such a result would indicate that it is not this aspect of the reaction which is incompatible with the acenaphthylenedione oxime ether (248). In practice, this reaction yielded a mixture, the mass spectrum of which gave no peak corresponding to the 'cross-over' product, the diphenylnaphthoxazine derivative (123). Flash-chromatography of the mixture gave only the expected 2,2-di-(4-methylphenyl)-2*H*-naphth[2,1-*b*]-1,4-oxazine (218a) albeit in poor yield (28%) together with a poor recovery of the 1,2-acenaphthylenedione oxime ether (248) (26%). It is likely therefore that the 1,2-acenaphthylenedione oxime ether (248) is more stable to cleavage than the naphthalenedione oxime ether (216a) and is hence unable to participate in a reaction analogous to that by which the naphthoxazine derivative (218a) was formed. The reason for this greater stability remains unclear while the nature of the fragments formed during the synthesis of the naphthoxazine derivative (218a) is unknown.

2.7 Ultraviolet/Visible Spectra and Photochromic Characteristics of Fused 2,2-Disubstituted 2*H*-1,4-Oxazines

Having synthesised a number of novel fused 2,2-diaryl-2*H*-1,4-oxazine derivatives and observed photochromism under ultraviolet irradiation (254 nm) during tlc, the photochromic behaviour of these compounds was investigated more thoroughly. The ultraviolet/visible spectra of the ring-closed form of each compound was first studied. The results detailed in Table 9 (Pages 112-114) were obtained using tetrahydrofuran solutions of each compound. Following the measurement of each spectrum, the solution was irradiated at 254 nm then the acquisition was promptly repeated. The absorptions in the visible region of the spectrum (400-750 nm) which resulted are assumed to be due to the ring-opened form of the 1,4-oxazine derivative and are labelled as such. No extinction coefficient is quoted for these absorptions in the visible region of the spectrum. As reversion to the bleached state begins on removal of the ultraviolet source, the observed intensity of the coloured form of each compound studied has more to do with the fade kinetics of a given species than its extinction coefficient. Indeed, certain of the compounds studied faded so rapidly that using the simple apparatus available, investigation of the coloured forms was impossible. Such cases are indicated by dashes in the column of the open form absorption maxima. Numbers in parentheses relate to studies carried out in the laboratories of Pittsburgh Plate Glass Industries (PPG). The ultraviolet/visible spectra of certain compounds were measured when cast into the acrylic polymer used by PPG for the production of ophthalmic lenses. The instrument designed at PPG allows irradiation at a

given wavelength while absorption of the sample at all other wavelengths is assessed. This procedure enables the coloured forms of even the most rapidly fading species to be observed.

In initial studies, the uv/visible spectrum of 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 24; (116)] was investigated. The spectrum of the ring-closed form shows two maxima in the ultraviolet region (257 and 317 nm) and no absorption bands in the visible region. This absence of colour under weak illumination is an essential feature of any photochromic agent with application in ophthalmic lenses. Following irradiation at 254 nm, the absorption maximum in the visible region was measured at 473 nm in tetrahydrofuran and at 475 nm in a polymer matrix. Solvatochromic effects, that is, variation in absorption characteristics due to interaction with solvent, are well known[2,3] and probably account for this 2 nm discrepancy. Other differences are likely to exist between the photochromic characteristics of 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazines in solution and imbibed into a polymer host. In general, the analogous diarylnaphthopyrans generally have faster activation and fade rates and lower colour intensity in solution than when in a polymer host.[68]

The absorption maxima in the ultraviolet spectrum of the ring-closed form of 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 29; (137a)] occur at similar wavelength but at higher intensity than those due to the diphenyl derivative [Scheme 24; (116)]. Van Gemert[68] reports that the presence of electron-donating para substituents on the phenyl rings of 3,3-

diphenyl-3*H*-naphtho[2,1-*b*]-1,4-pyran (116; CH for N) results in a bathochromic shift (a shift to longer wavelength) in the visible spectrum of its ring-opened form. Examination of the ultraviolet/visible spectrum of the di-(4-methylphenyl)naphthoxazine derivative [Scheme 29; (137a)] reveals a similar shift with respect to the parent diphenyl compound (116). Thus the visible absorption due to the ring-opened form of the di-(4-methylphenyl)naphthoxazine derivative (138a) gives rise to a maximum at 495 nm. It has also been observed[68] that the di-(4-methoxyphenyl)naphthopyran [Scheme 39; (172; CH for N)] exhibits a much faster fade rate and has a visible absorption maximum bathochromically shifted 48 nm with respect to the diphenyl compound [Scheme 24; (116; CH for N)]. In the light of these observations it is not surprising that the coloured form of the 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 39; (172)] reverted to the bleached state too rapidly for measurements to be taken. However, examination of its visible spectrum in a more sophisticated instrument revealed an absorption maximum at 510 nm, a bathochromic shift of 35 nm from that of the diphenyl compound (116). It should also be noted that the ring-closed form of the di-(4-methoxyphenyl)naphthoxazine derivative (172) also exhibits three maxima in its ultraviolet spectrum.

Strong absorption in the near ultraviolet region is an important characteristic of any potential ophthalmic photochromic material. As sunlight contains very little ultraviolet radiation of wavelength shorter than 300 nm, it is the near

ultraviolet radiation which must be absorbed to elicit the photochromic response.

By drawing analogy once again from the corresponding naphthopyran, the spirofluorenylnaphthoxazine derivative [Scheme 44; (197)] would be expected to exhibit a more intensely coloured and slower fading ring-opened form than the previously mentioned non-spiro derivatives [eg Scheme 24; (116)]. While information on the fade kinetics of the compounds prepared during these studies has not yet been released by PPG, the fade rate of the spirofluorenylnaphthoxazine derivative (197) was sufficiently slow to allow measurement of a visible absorption band (475 nm) which was very similar to that of the diphenyl compound (116) (473 nm). It is noteworthy that the ring-closed form of the spirofluorenylnaphthoxazine derivative (197) gives an absorption maximum well into the near ultraviolet region (354 nm).

The ultraviolet/visible spectra of the 3,3-diaryl-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazines [Scheme 45; (202)] were next investigated. The results are described with respect to 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 24; (116)]. The methoxy substituent of 3,3-diphenyl-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202a) causes a small hypsochromic shift in the visible spectrum of its ring-opened form (203a) giving an absorption maximum which was measured in tetrahydrofuran solution and acrylic at 467 and 469 nm respectively. A similarly modest hypsochromic shift (6 nm) can be observed on the introduction of a 9-methoxy substituent in the analogous

diphenylnaphthopyran.[68] Comparison[82] of the ultraviolet/visible absorption spectrum of 1,3,3-trimethylspiro[indoline-2,3'-[3*H*]-naphth[2,1-*b*]-1,4-oxazine] [Scheme 12; (58)] and its 9'-methoxy derivative reveals that while the presence of the methoxy substituent has very little effect on the visible absorption maximum, the photochromic response (rate of change of optical density) is greatly enhanced. While a similarly enhanced photochromic response is expected for the diphenylmethoxynaphthoxazine derivative (202a) measurement of this property was not possible using the apparatus available.

Comparison of the ring-opened form of the diphenylmethoxynaphthoxazine derivative (203a) with that of 3,3-di-(4-methylphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (203b) reveals a 16 nm bathochromic shift in the visible spectrum of the latter. A further bathochromic shift was expected in the visible spectrum of the coloured form (203c) of 3,3-di-(4-methoxyphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202c). Unfortunately, the rapid fade rate of (203c) prevented its visible spectrum being measured. While the accelerated fading of the ring-opened form (203c) is likely to be the result of electron-donating methoxy groups on the two phenyl substituents, a further increase in fade rate may be caused by a steric interaction between the 9-methoxy group and the methoxyphenyl moieties destabilising the *anti* quinonoidal form (203c).

It was anticipated that investigation of the ultraviolet/visible spectra of the 2,2-diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazines [Scheme 48; (218)] would be much more straightforward than those of the foregoing compounds. Comparison of the

photochromic characteristics of a given 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyran with an identically substituted 3*H*-naphtho[2,1-*b*]pyran reveals a much greater stability in the ring-opened structure of the former.[68] As has been described (see Page 74) 2,2-diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazines (218) would also be expected to give comparatively stable ring-opened forms (219). The parent diphenyl compound [Scheme 26; (123)] was previously studied by Gentex and was found to give a very poor photochromic response. However, measurement was possible of the visible spectra of both of the naphth[1,2-*b*]-1,4-oxazine derivatives isolated in high purity during these studies. The ultraviolet spectrum of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) shows two absorption maxima. On irradiation at 254 nm, an absorption in the visible region was measured at 497 nm in tetrahydrofuran solution and at 502 nm in a polymer host. The ultraviolet spectrum of the ring-closed form of 2,2-di-(4-methoxyphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218d) also contains two absorption maxima, the weaker of which absorbs longer wavelengths than the corresponding band due to the di-(4-methylphenyl) derivative (218a). The visible absorption maximum (534 nm) of the ring-opened form of (218d) is similarly bathochromically shifted.

The ultraviolet spectra of the 2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines [Scheme 51; (232)] each show three maxima due to their ring-closed forms. The diphenyl (232a), the di-(4-methylphenyl) (232b) and the di-(4-methoxyphenyl) (232e) derivatives give similar absorptions at around 255, 350 and 375 nm and hence absorb significantly longer wavelengths than the

similarly substituted naphthoxazine derivatives previously described. However, 2,2-di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232c) absorbs at much shorter wavelengths (258, 305 and 344 nm) than the other phenanthro-oxazine derivatives. The visible spectra of the ring-opened forms of the phenanthro-oxazine derivatives (232) give maxima which differ according to the nature of the functionalities in the para position of the diaryl substituents. Thus, irradiation of a tetrahydrofuran solution of the diphenylphenanthro-oxazine derivative (232a) gives a visible absorption maximum at 450 nm (474 nm in acrylic). Relative to the diphenyl compound (232a), the visible absorption of the di-(4-methylphenyl) derivative (232b) is bathochromically shifted by 17 nm to 467 nm. A further bathochromic shift is observed due to the ring-opened form of 2,2-di-(4-methoxyphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232e) whose absorption maximum was measured at 497 nm in tetrahydrofuran and 519 nm in acrylic. The presence of the electron-withdrawing trifluoromethyl substituents explains the visible spectrum of the ring-opened form of 2,2-di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232c) whose maximum (429 nm) is hypsochromically shifted with respect to the diphenyl compound (232a).

Comparison was next made between 3,3-diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazines [eg Scheme 29; (137)] and the 3,3-diaryl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazines [Scheme 57; (244)]. Similar comparisons have been made between spirooxazines[82] and fused benzopyrans[68] fused to naphthalene and quinoline nuclei. These studies suggest that the major effect of the presence of the

extra nitrogen in the pyridobenzoxazine ring system of (244) would be to increase the rate of activation of the photochromic species with little difference being observed in the visible absorption maxima. In practice, while the ring-closed forms of the pyridobenzoxazine derivatives (224) gave similar ultraviolet spectra, rapid fading made measurement of the visible absorption of their ring-opened forms very difficult. 3,3-Diphenyl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine (244a), the only pyridobenzoxazine derivative whose visible absorption could be measured, gave a maximum (475 nm) coincident with that of 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116). Information on the coloration and fade rates of the other pyridobenzoxazine derivatives (224) prepared during these studies has not yet been released by PPG.

The foregoing chapter has demonstrated that several novel fused 2*H*-1,4-oxazine derivatives are accessible through the extension of methodology developed previously at Edinburgh.[137] Where the oxazine derivatives were obtained in quantities sufficient for study, photochromism was observed. A more in-depth characterisation of the photochromic properties and fatigue resistance of each derivative is now required.

Table 7: Ultraviolet-Visible Spectroscopic Data

Compound	Ring-closed form						Open form
	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm
3,3-Diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116)	257	14412	317	8256			473 (475)
3,3-Di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a)	247	20381	317	8387			495
3,3-Di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172)	247	20199	323	5846	349	4423	---- (510)
3,3-Spirofluoren-9-yl-3*H*-naphth[2,1-*b*]-1,4-oxazine (197)	267	14567	325	4763	354	3578	475
3,3-Diphenyl-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202a)	238	49418	340	6999			467 (469)
3,3-Di-(4-methylphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202b)	257	15239	336	7934			483
3,3-Di-(4-methoxyphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202c)	250	31302	339	8070			----

Spectra were recorded in tetrahydrofuran solution or, for values in parentheses, in cast acrylic.

Table 7: Ultraviolet-Visible Spectroscopic Data (cont.)

Compound	Ring-closed form						Open form
	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm
2,2-Di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a)	253	21827	321	4478			497 (502)
2,2-Di-(4-methoxyphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218d)	255	22737	353	2611			534 (534)
2,2-Diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a)	255	35408	351	6181	375	4701	450 (474)
2,2-Di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b)	258	28827	350	6138	375	4699	467
2,2-Di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232c)	258	33638	305	14122	344	2754	429

Spectra were recorded in tetrahydrofuran solution or, for values in parentheses, in cast acrylic.

Table 7: Ultraviolet-Visible Spectroscopic Data (cont.)

Compound	Ring-closed form						Open form
	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm
2,2-Di-(4-methoxyphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232e)	254	37580	346	6352	375	5045	497 (519)
3,3-Diphenyl-3*H*-[1,4]oxazino[3,2-*f*]quinoline (244a)	251	17099	315	7027	345	3732	475
3,3-Di-(4-methylphenyl)-3*H*-[1,4]oxazino[3,2-*f*]quinoline (244b)	248	18113	316	7114	345	3832	----
3,3-Di-(4-methoxyphenyl)-3*H*-[1,4]oxazino[3,2-*f*]quinoline (244c)	254	14943	315	7095	346	3825	----

Spectra were recorded in tetrahydrofuran solution or, for values in parentheses, in cast acrylic.

2.8 EXPERIMENTAL

General Experimental Details

Infrared spectra were recorded using a Perkin-Elmer Paragon 1000 Fourier-Transform spectrophotometer or a Bio-Rad FTS-7 Fourier-Transform spectrophotometer and bands were strong and sharp unless specified as w (weak) or br (broad). Solids were measured as suspensions (mulls) in Nujol and liquids as thin films.

^{1}H nmr spectra were measured in the stated solvent at 200 MHz using a Varian Gemini instrument or a Bruker AC-200 instrument, at 250 MHz using a Bruker AC-250 instrument, or at 360 MHz using a Bruker WH-360 instrument. Signals were sharp unless specified as br (broad); s = singlet, d = doublet, dd = double doublet, ddd = double double doublet, t = triplet, q = quartet and m = multiplet. ^{13}C nmr spectra were measured in the stated solvent at 50 MHz using a Bruker AC-200 instrument, at 62.5 MHz using a Bruker AC-250 instrument or at 90 MHz using a Bruker WH-360 instrument and were fully decoupled. Signals were sharp and quat = quaternary carbon atom. Quaternary carbon atoms and methylene groups were identified by $3\pi/4$ DEPT (Distortionless Enhancement by Polarisation Transfer) pulse sequence spectra.

Electron Impact (EI) mass spectra were recorded at 70 eV on Finegan Quad 4600 and Kratos MS-50TC instruments. Fast Atom Bombardment (FAB) mass spectra were recorded at 7 keV on a Kratos MS-50TC instrument for matrices in thioglycerol and 3-nitrobenzyl alcohol. Atmospheric Pressure

Chemical Ionisation (APCI) mass spectra were recorded on Thermoquest LCQ and Micromass Platform II instruments.

X-ray diffraction data were collected using a Stoe-Stadi four circle diffractometer on single crystals grown from the stated crystallisation solvent.

Ultraviolet spectra were recorded in anhydrous tetrahydrofuran using a Perkin-Elmer Lambda 11 uv/visible spectrophotometer. Further uv/visible spectra were recorded in an 2,2'-azodi-(2-methylpropanenitrile) initiated copolymer of bisphenol dimethacrylate - polyethylene glycol dimethacrylate (4:1) on an instrument custom built by Pittsburgh Plate Glass Industries (PPG).

Elemental analyses were determined using a Perkin-Elmer 2400 elemental analyser. Routine melting points (mp) were carried out using a Gallenkamp apparatus and are uncorrected. Melting points of analytical samples were determined using a Kofler hot-stage apparatus and are uncorrected.

All reagents were laboratory grade unless specified. Sodium hydride was a 60% dispersion in mineral oil and was washed with anhydrous ether before use. Activated manganese dioxide was supplied by Aldrich (cat. no. 21,764-6). Grignard reactions used magnesium turnings supplied by Aldrich (cat. no. 20,090-5).

Solvents were of technical grade unless otherwise stated and light petroleum had bp 60-80°C. Anhydrous solvents were dried as follows. Acetonitrile, dimethylformamide, dichloromethane and chloroform were distilled and stored over anhydrous 4Å molecular sieves. 1,4-Dioxane and 1,2-dimethoxyethane were distilled from calcium hydride and stored over 4Å molecular sieves. Xylene was distilled and stored over sodium wire. Ether and toluene were dried with sodium wire. Ethanol was distilled from magnesium and iodine and stored over 4Å molecular sieves. Tetrahydrofuran was distilled from sodium and benzophenone and stored over 4Å molecular sieves.

Organic extracts were dried over anhydrous magnesium sulphate prior to filtration and rotary evaporation under reduced pressure.

Wet column flash-chromatography was carried out over silica (Fluka Kieselgel 60, 220-440 mesh). Thin layer chromatography (tlc) was carried out using Polygram SIL G/UV_{254} precoated plastic sheets.

Elemental Analyses and Mass Spectroscopic Data

Elemental analyses and mass spectroscopic data are collected in Table 8, Pages 251-255.

7-Methoxy-2-naphthol (205)

(a) A stirred suspension of sodium hydride (1.3 g; 0.055 mol) in anhydrous dimethylformamide (20.0 ml) was cooled to 10°C (ice-water bath) then treated

dropwise with a solution of 2,7-dihydroxynaphthalene (204) (8.0 g; 0.05 mol) in anhydrous dimethylformamide (20.0 ml). The resulting suspension of a beige solid in a brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min then was treated in one portion with a solution of dimethyl sulphate (6.3 g; 0.05 mol) in anhydrous dimethylformamide (10.0 ml). The resulting mixture was then stirred at 100°C (oil bath) with the exclusion of atmospheric moisture for 1 h.

The resulting brown solution was cooled to room temperature and treated with water (15.0 ml), stirred for 15 min then rotary evaporated under high vacuum (oil pump). The residue was treated with water (100 ml) and the mixture was acidified with 2M aqueous hydrochloric acid then extracted several times with dichloromethane to give a partially crystalline brown gum (11.4 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 2,7-dimethoxynaphthalene (206) (1.7 g; 18%) which formed colourless microcrystals, mp 135-137°C [from light petroleum (bp 80-100°C)] (lit,[157] 139°C), δ_H ($CDCl_3$) 7.66-7.63 (2H, m, ArH), 7.06-6.96 (4H, m, ArH) and 3.90 (6H, s, 2 x CH_3).

Further elution with hexane-ether (9:1) gave a mixture of 2,7-dimethoxynaphthalene (206) and 7-methoxy-2-naphthol (205) (1.1 g).

Further elution with hexane-ether (9:1) gave 7-methoxy-2-naphthol (205) (2.5 g; 29%) which formed colourless microcrystals, mp 117-118°C [from toluene-light petroleum (bp 80-100°C)] (lit,[151] 116-117°C), ν_{max} 3500-3000 br (OH) cm^{-1}, δ_H ($CDCl_3$) 7.66 (2H, d, J 8.7 Hz, ArH), 7.05-6.92 (4H, m, ArH), 5.36 (1H, s, OH) (exch) and 3.89 (3H, s, CH_3).

Elution with ether gave 2,7-dihydroxynaphthalene (204) as a cream solid (2.0 g; 25%), mp 181°C (decomp) [lit,[157] 190°C (decomp)], identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

(b) Anhydrous potassium carbonate (4.2 g; 0.03 mol) was added at room temperature to a stirred solution of 2,7-dihydroxynaphthalene (204) (8.0 g; 0.05 mol) in Analar acetone (37.5 ml) and the suspension was stirred under nitrogen at room temperature for 1 h.

The resulting suspension of a colourless solid in a green solution was treated in one portion with a solution of dimethyl sulphate (6.9 g; 0.055 mol) in Analar acetone (12.5 ml) and the mixture was stirred and heated under reflux under nitrogen for 15 h.

The suspension was rotary evaporated and the residue treated with dichloromethane (100 ml). The insoluble green solid (9.7 g) was collected, dissolved in warm water (75.0 ml) and the solution acidified with 2M aqueous

hydrochloric acid then extracted several times with ethyl acetate to give impure 2,7-dihydroxynaphthalene (204) as a tacky green solid (1.1 g; 14%) identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

The dichloromethane mother liquor was rotary evaporated and the pale green gummy residue (8.3 g) flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,7-dimethoxynaphthalene (206) as a colourless solid (2.9 g; 31%), mp 137-140°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

Further elution with hexane-ether (19:1) gave 7-methoxy-2-naphthol (205) as a colourless solid (3.5 g; 40%), mp 113-115°C, identified by comparison [mp, ir and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(c) Anhydrous potassium carbonate (8.8 g; 0.0625 mol) was added at room temperature to a stirred solution of 2,7-dihydroxynaphthalene (204) (8.0 g; 0.05 mol) in Analar acetone (37.5 ml) and the resulting suspension was stirred at room temperature under nitrogen for 1h.

The stirred suspension was treated in one portion with a solution of dimethyl sulphate (6.9 g; 0.055 mol) in Analar acetone (12.5 ml) and the resulting suspension was stirred and heated under reflux under nitrogen for 15 h.

The resulting suspension of a pale green solid in a green solution was rotary evaporated and the residue treated with dichloromethane (100 ml). The insoluble green solid was collected and dissolved in warm water (75.0 ml) and the solution acidified with 2M aqueous hydrochloric acid then extracted several times with ethyl acetate. The ethyl acetate extracts were combined with the original dichloromethane extract and rotary evaporated to give a gummy beige solid (9.4 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,7-dimethoxynaphthalene (206) (2.7 g; 29%) as a colourless solid, mp 139-140°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

Further elution with hexane-ether (19:1) gave 7-methoxy-2-naphthol (205) (3.2 g; 37%) as a colourless solid, mp 116-117°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(d) Anhydrous potassium carbonate (8.2 g; 0.0625 mol) was added in one portion at room temperature to a solution of 2,7-dihydroxynaphthalene (204)

(8.0 g; 0.05 mol) in Analar acetone (37.5 ml) and the resulting suspension was stirred at room temperature under nitrogen for 1 h.

The resulting suspension of a colourless solid in a brown solution was treated in one portion at room temperature with a solution of methyl iodide (7.8 g; 0.055 mol) in Analar acetone (12.5 ml) and the mixture was then stirred at room temperature under nitrogen for 16 h.

The resulting suspension of a grey solid in a green solution was rotary evaporated and the residue treated with dichloromethane (100 ml). The insoluble green solid (16.0 g) was collected, dissolved in warm water (75.0 ml) and the stirred solution acidified with 2M aqueous hydrochloric acid, then extracted several times with ethyl acetate to give impure 2,7-dihydroxynaphthalene (204) (1.5 g; 19%), mp 145-150°C, identified by comparison [ir spectrum and tlc in hexane-ether (2:3) over silica] with an authentic sample.

The dichloromethane mother liquor was rotary evaporated and the resulting gummy beige solid (8.2 g) was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,7-dimethoxynaphthalene (206) (1.5 g; 16%), mp 134-136°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

Further elution with hexane-ether (19:1) gave 7-methoxy-2-naphthol (205) as a colourless solid (3.0 g; 34%), mp 116-118°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

7-Methoxy-1,2-naphthalenedione 1-Oxime (207)

A stirred solution of 7-methoxy-2-naphthol (205) (3.0 g; 0.017 mol) in glacial acetic acid (21.5 ml) was cooled to 10°C (ice-water bath) and treated dropwise at <10°C over 30 min with a solution of sodium nitrite (1.2 g; 0.017 mol) in water (8.5 ml). The resulting red-brown solution was stirred at <10°C for 1 h and then at room temperature for 2 h.

The resulting red-brown suspension was concentrated by rotary evaporation to one third of the original volume, then treated with water (13.0 ml). The insoluble red solid (3.6 g) was collected and crystallised from toluene-light petroleum (bp 80-100°C) with hot filtration to remove some insoluble material, to give the methoxynaphthalenedione oxime (207) as a red solid (2.6 g; 74%), mp 127-129°C (lit,[151] 124-125°C), ν_{max} 1621 (C=N) cm^{-1}.

6-Methoxy-2-naphthol (209)

(a) A stirred suspension of sodium hydride (0.53 g; 0.022 mol) in anhydrous dimethylformamide (8.0 ml) was cooled to 10°C (ice-water bath) then treated dropwise with a solution of 2,6-dihydroxynaphthalene (208) (3.2 g; 0.02 mol) in anhydrous dimethylformamide (8.0 ml). The suspension was

stirred at room temperature for 15 min then treated in one portion with a solution of dimethyl sulphate (2.5 g; 0.02 mol) in anhydrous dimethyl-formamide (4.0 ml). The resulting mixture was then stirred at 100°C (oil bath) with the exclusion of atmospheric moisture for 1 h.

The resulting purple-brown solution was cooled to room temperature, treated with water (6.0 ml) and stirred for 15 min. The mixture was then rotary evaporated under high vacuum (oil pump) and the residue treated with water (40.0 ml) and the resulting suspension acidified with 2M aqueous hydrochloric acid then extracted several times with dichloromethane to give a gummy beige solid (2.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,6-dimethoxynaphthalene (210) as a colourless solid (0.2 g; 19%), mp 155-158°C (lit,[158] 149-151°C).

Further elution with hexane-ether (19:1) gave 6-methoxy-2-naphthol (209) as a colourless solid (0.89 g; 26%), mp 152-155°C (lit,[152] 150-152°C), ν_{max} 3500-3100 br (OH) cm^{-1}.

(b) A stirred suspension of sodium hydride (1.1 g; 0.044 mol) in anhydrous dimethylformamide (8.0 ml) was cooled to 10°C (ice-water bath) then treated dropwise with a solution of 2,6-dihydroxynaphthalene (208) (3.2 g; 0.02 mol) in anhydrous dimethylformamide (8.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min. The

resulting suspension was treated in one portion with a solution of dimethyl sulphate (2.5 g; 0.02 mol) in anhydrous dimethylformamide (4.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 2 h.

The resulting green suspension was treated with water (6.0 ml) and stirred at room temperature for 15 min then rotary evaporated under high vacuum (oil pump). The residue was treated with water (40.0 ml) and the resulting suspension acidified with 2M aqueous hydrochloric acid then extracted several times with dichloromethane to give a gummy red solid (3.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,6-dimethoxynaphthalene (210) as a colourless solid (1.3 g; 17%), identical [mp, ir spectrum and tlc in hexane-ether (2:3) over silica] with a sample obtained in (a) before.

Further elution with hexane-ether (19:1) gave 6-methoxy-2-naphthol (209) as a colourless solid (0.72 g; 21%), mp 152-153°C, identical [mp, ir and tlc in hexane-ether (2:3) over silica] with a sample obtained in (a) before.

The Attempted Reaction of 6-Methoxy-2-naphthol (209) with Sodium Nitrite in the Presence of Acetic Acid

A stirred solution of 6-methoxy-2-naphthol (209) (1.7 g; 0.01 mol) in glacial acetic acid (25.0 ml) was cooled to 10°C (ice-water bath) and treated dropwise

over 30 min with a solution of sodium nitrite (0.69 g; 0.01 mol) in water (5.0 ml). The resulting red-brown solution was stirred at <10°C for 1 h then at room temperature for 2 h.

The red-brown solution was concentrated by rotary evaporation to one third of the original volume, then treated with water (10.0 ml) and the resulting suspension was filtered to give a product presumed to be 6-methoxy-1,2-naphthalenedione 1-oxime (211) as a brown solid (1.8 g; 89%) which was used without further purification.

1,2-Naphthalenedione 1-Oxime Lithium Salt (112)

A stirred solution of 1,2-naphthalenedione 1-oxime (107) (86.5 g; 0.5 mol) in Analar acetone (1250 ml) was treated dropwise at room temperature with a solution of lithium hydroxide monohydrate (21.0 g; 0.5 mol) in water (250 ml) and the resulting green suspension was stirred at room temperature for 30 min.

The green suspension was filtered to give a green solid which was washed with acetone and combined with a second crop obtained by rotary evaporation of the aqueous acetone mother liquor and washing the residual solid with acetone to give the lithium salt (112) as metallic green microplates (total 89.5 g; 100%), mp 251°C (decomp with gas evolution) (lit,[137] 263-267°C), ν_{max} 3700-3300 br and 3217 (OH) and 1620 (C=O) cm^{-1}, which was used without further purification.

7-Methoxy-1,2-naphthalenedione 1-Oxime Lithium Salt (198)

A stirred solution of 7-methoxy-1,2-naphthalenedione 1-oxime (207) (2.8 g; 0.014 mol) in Analar acetone (35.0 ml) was treated in one portion with a solution of lithium hydroxide monohydrate (0.59 g; 0.014 mol) in water (7.0 ml) and the resulting green-brown suspension was stirred at room temperature for 30 min.

The green-brown suspension was rotary evaporated and the residue was treated with acetone (10.0 ml). The insoluble solid was collected to give the lithium salt (198) as a brown solid (2.9 g; 99%), mp 247°C (decomp), which was used without further purification.

The Attempted Reaction of the Presumed 6-Methoxy-1,2-naphthalene-dione 1-Oxime (211) with Lithium Hydroxide

A stirred solution of the presumed 6-methoxy-1,2-naphthalenedione 1-oxime (211) (1.0 g; 0.005 mol) in Analar acetone (12.5 ml) was treated in one portion at room temperature with a solution of lithium hydroxide monohydrate (0.21 g; 0.005 mol) in water (2.5 ml), and the resulting brown solution was stirred at room temperature for 30 min.

The brown solution was rotary evaporated to give a gummy brown solid (1.3 g) which was used without further purification.

1,1-Diaryl-2-ethoxy-1-hydroxyethanes (131)

Grignard grade magnesium turnings (7.2 g; 0.3 g atom) were added to a stirred solution of the corresponding aryl bromide (0.1 mol) in anhydrous tetrahydrofuran (25.0 ml). The stirred mixture refluxed spontaneously with or without the addition of a few drops of ethyl bromide and was treated dropwise with a further solution of the aryl bromide (0.2 mol) in anhydrous ether (60.0 ml) added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool and then was treated dropwise at room temperature with a solution of ethyl 2-ethoxyacetate (129) (13.2 g; 0.1 mol) in anhydrous ether (15.0 ml). After the initial vigorous reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

After being allowed to cool, the mixture was treated cautiously with ice (150 g) and 2M aqueous sulphuric acid (150 ml; 0.3 mol) and the resulting mixture stirred for 15 min, then the layers separated and worked-up for the individual reactions below.

(a) The aqueous layer from the reaction with 4-bromotoluene (127a) was extracted several times with ether and the combined ether extracts were rotary evaporated to give 1,1-di-(4-methylphenyl)-2-ethoxy-1-hydroxyethane (131a) as a pale yellow oil (100%), ν_{max} 3556 and 3476 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.35-7.09 (8H, m, ArH), 3.92 (2H, s, CH_2), 3.61 (2H, q, J 7.0 Hz, CH_2), 3.60-3.10

(1H, brs, OH) (exch), 2.32 (6H, s, 2 x CH_3) and 1.21 (3H, t, J 7.0 Hz, CH_3), which could not be purified without decomposition.

(b) The aqueous layer from the reaction with 4-bromobenzotrifluoride (127b) was extracted several times with ether and the combined ether extracts were rotary evaporated to give a red-brown oil, distillation of which afforded 1,1-di-(4-trifluoromethylphenyl)-2-ethoxy-1-hydroxyethane (131b) as a colourless oil (89%), bp 180°C/0.04 mm Hg, ν_{max} 3466 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.61-7.50 (8H, m, ArH), 3.95 (2H, s, CH_2), 3.64 (2H, q, J 7.2 Hz, CH_2), 1.57 (1H, s, OH) (exch) and 1.22 (3H, t, J 7.2 Hz, CH_3).

(c) The aqueous layer from the reaction with 4-bromo-*N,N*-dimethylaniline (127c) was extracted several times with ether and the combined ether extracts discarded. The stirred aqueous mother liquor was cooled (ice bath) and treated portionwise with 20% w/v aqueous sodium hydroxide solution until just basic then extracted several times with ether. The combined ether extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give a gummy pale brown solid trituration of which with light petroleum afforded 1,1-di-(4-*N,N*-dimethylaminophenyl)-2-ethoxy-1-hydroxyethane (131c) (78%) which formed cream microcrystals, mp 105-107°C (from light petroleum), ν_{max} 3377 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.33-7.25 (4H, m, ArH), 6.74-6.67 (4H, m, ArH), 3.89 (2H, s, CH_2), 3.62 (2H, q, J 7.0 Hz, CH_2), 3.57 (1H, s, OH) (exch), 2.94 (12H, s, 4 x CH_3) and 1.22 (3H, t, J 7.0 Hz, CH_3).

(d) The aqueous layer from the reaction with 1-bromo-2,4-dimethylbenzene (173) was extracted several times with ether and the combined ether extracts were rotary evaporated to give an amber oil, distillation of which afforded 1,1-di-(2,4-dimethylphenyl)-2-ethoxy-1-hydroxyethane (175) as a colourless oil (76%), bp 124°C/0.026 mm Hg, ν_{max} 3550 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.44 (2H, d, J 8.0 Hz, ArH), 7.01-6.96 (4H, m, ArH), 3.90 (2H, s, CH_2), 3.64 (2H, q, J 7.1 Hz, CH_2), 3.40 (1H, s, OH) (exch), 2.29 (6H, s, 2 x CH_3), 1.98 (6H, s, 2 x CH_3) and 1.25 (3H, t, J 7.1 Hz, CH_3).

(e) The aqueous layer from the reaction with 1-bromonaphthalene (180) was extracted several times with ether. The combined ether extracts precipitated a solid which was collected and combined with further material obtained by rotary evaporating the ether layer and triturating the residue obtained with light petroleum to give 1,1-di-(naphth-1-yl)-2-ethoxy-1-hydroxyethane (182) as a colourless solid (total 64%), mp 134-135°C (from toluene-light petroleum), ν_{max} 3534 (OH) cm^{-1}, δ_H ($CDCl_3$) 8.57 (2H, d, J 8.5 Hz, ArH), 7.87-7.80 (6H, m, ArH), 7.49-7.25 (6H, m, ArH), 4.89 (2H, s, CH_2), 4.06 (1H, s, OH) (exch), 3.72 (2H, q, J 7.0 Hz, CH_2) and 1.32 (3H, t, J 7.0 Hz, CH_3).

The light petroleum filtrate was rotary evaporated to give a yellow oil which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) gave an oily colourless solid which was washed with light petroleum to give naphthalene as a colourless solid, mp

126-130°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (3:7) over silica] with an authentic sample.

Elution with hexane-dichloromethane (3:2) gave a further crop of the tertiary alcohol (182) as a colourless solid (12%), mp 126-130°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (3:7) over silica] with a sample prepared before.

1,1-Di-(4-methoxyphenyl)-2-ethoxyethene (130d)

Magnesium turnings (7.2 g; 0.3 g atom) were added to a stirred solution of 4-bromoanisole (127d) (18.7 g; 0.1 mol) in anhydrous tetrahydrofuran (25.0 ml) followed by ethyl bromide (3 drops). The stirred mixture refluxed spontaneously and was treated dropwise with a further solution of 4-bromoanisole (127d) (37.4 g; 0.2 mol) in anhydrous ether (60.0 ml) added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool and treated dropwise at room temperature with a solution of ethyl 2-ethoxyacetate (129) (13.2 g; 0.1 mol) in anhydrous ether (15.0 ml). After the initial vigorous exothermic reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

After being allowed to cool, the mixture was treated cautiously with ice (150 g) and 2M aqueous sulphuric acid (150 ml; 0.3 mol) then stirred for 15 min. The

layers were separated and the aqueous layer extracted with ether. Rotary evaporation of the combined ether extracts gave a yellow-brown oil (34.4 g). This was triturated with light petroleum to give the enol ether (130d) (17.5 g; 62%) which formed colourless microcrystals, mp 72-73°C (from light petroleum), δ_H ($CDCl_3$) 7.49-7.43 (2H, m, ArH), 7.26-7.20 (2H, m, ArH), 6.99-6.87 (4H, m, ArH), 6.45 (1H, s, CH), 4.01 (2H, q, J 7.1 Hz, CH_2), 3.84 (6H, s, 2 x CH_3) and 1.40 (3H, t, J 7.1 Hz, CH_3).

Rotary evaporation of the light petroleum mother liquor gave an orange-brown oil (14.4 g) which was investigated no further.

2,2-Diarylacetaldehydes

(a) The corresponding 1,1-diaryl-2-ethoxy-1-hydroxyethane (0.04 mol) was treated with 85% v/v aqueous formic acid (40.0 ml) and the resulting dispersion was stirred and heated under reflux for 6 h.

The dispersion was poured into water (500 ml) and extracted several times with ether. The combined ether extracts were washed several times with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated and the crude oily or solid product was purified as described for the individual reactions below.

(i) 1,1-di-(4-methylphenyl)-2-ethoxy-1-hydroxyethane (131a) afforded the known[140] 2,2-di-(4-methylphenyl)acetaldehyde (133a) as a pale yellow oil

(67%), bp 156°C/0.02 mm Hg, ν_{max} 2721 (CH=O) and 1723 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.94 (1H, d, J 2.5 Hz, CH=O), 7.24-7.11 (8H, m, ArH), 4.85 (1H, d, J 2.4 Hz, CH) and 2.37 (6H, s, 2 x CH_3).

(ii) 1,1-Di-(4-trifluoromethylphenyl)-2-ethoxy-1-hydroxyethane (131b) afforded 2,2-di-(4-trifluoromethylphenyl)acetaldehyde (133b) as a pale orange oil (78%), ν_{max} 2726 (CH=O) and 1729 (C=O) cm^{-1}, δ_H 9.98 (1H, d, J 1.7 Hz, CH=O), 7.85-7.14 (8H, m, ArH) and 4.98 (1H, s, CH), which decomposed on attempted purification.

(iii) 1,1-Di-(2,4-dimethylphenyl)-2-ethoxy-1-hydroxyethane (175) afforded 2,2-di-(2,4-dimethylphenyl)acetaldehyde (177) as a colourless oil (87%), bp 150°C/0.008 mm Hg, ν_{max} 2716 (CH=O) and 1724 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.98 (1H, d, J 1.7 Hz, CH=O), 7.08-6.99 (4H, m, ArH), 6.86 (2H, d, J 7.8 Hz, ArH), 5.13 (1H, d, J 1.6 Hz, CH), 2.33 (6H, s, 2 x CH_3) and 2.26 (6H, s, 2 x CH_3).

(b) A stirred solution of 1,1-di-(4-trifluoromethylphenyl)-2-ethoxy-1-hydroxyethane (131b) (0.72 g; 0.0019 mol) in 1,2-dimethoxyethane (15.0 ml) was treated with 20% w/v aqueous hydrochloric acid (5.0 ml) added in one portion. The colourless heterogeneous mixture was stirred vigorously and heated under reflux for 1.5 h.

The mixture was cooled then concentrated by rotary evaporation to one quarter of the original volume then extracted several times with ether to give the

unreacted tertiary alcohol (131b) as a red-brown oil (0.61 g; 85%) identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

(c) Repetition of the reaction described in (b) but using 1,4-dioxane instead of 1,2-dimethoxyethane as solvent gave, after work-up, the unreacted tertiary alcohol (131b) as a brown oil (100%) identified by comparison [ir and ^{1}H nmr spectra and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

(d) 1,1-Di-(4-*N,N*-dimethylaminophenyl)-2-ethoxy-1-hydroxyethane (131c) (1.9 g; 0.0058 mol) was treated with 85% v/v aqueous formic acid (30.0 ml) and the resulting solution was stirred and heated under reflux for 6 h.

The solution was cooled and concentrated by rotary evaporation under high vacuum (oil pump), then poured into water (30.0 ml) and washed several times with ether and the washings discarded. The stirred aqueous mother liquor was cooled (ice bath) then treated portionwise with solid sodium hydrogen carbonate until just basic, then extracted several times with ether to give the 2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (133c) as a pale green solid (1.4 g; 86%), mp 78-82°C, ν_{max} 2717 (CH=O) and 1714 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.77 (1H, d, J 3.0 Hz, CH=O), 7.13-6.98 (4H, m, ArH), 6.67-6.63 (4H, m, ArH), 4.62 (1H, d, J 2.8 Hz, CH), 2.88 (6H, s, 2 x CH_3) and 2.86 (6H, s, 2 x CH_3), which decomposed on attempted purification.

(e) 1,1-Di-(naphth-1-yl)-2-ethoxy-1-hydroxyethane (182) (13.7 g; 0.04 mol) was treated with 85% v/v aqueous formic acid (40.0 ml) and the resulting dispersion was stirred and heated under reflux for 15 h.

The dispersion was poured into water (200 ml) and extracted twice with ether (2 x 20.0 ml). The resulting three-phase mixture was filtered to give the aldehyde (184) (9.2 g; 78%) which formed colourless needles, mp 189-190°C (from toluene), ν_{max} 2725 (CH=O) and 1725 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.25 (1H, d, J 2.1 Hz, CH=O), 7.98-7.85 (6H, m, ArH), 7.58-7.39 (6H, m, ArH), 7.29-7.22 (2H, m, ArH) and 6.41 (1H, d, J 1.9 Hz, CH).

The ether-aqueous filtrate was separated and the aqueous layer further extracted several times with ether. The combined extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution, then rotary evaporated to give a complex brown gum (1.8 g), which yielded no identifiable material.

(f) Grignard grade magnesium turnings (7.2 g; 0.3 g atom) were added to a stirred solution of the corresponding aryl bromide (0.1 mol) in anhydrous tetrahydrofuran (25.0 ml). The stirred mixture refluxed spontaneously with or without the addition of a few drops of ethyl bromide, then was treated dropwise with a further solution of the aryl bromide (0.2 mol) in anhydrous ether (60.0 ml), added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool then was treated dropwise at room temperature with a solution of ethyl 2-ethoxyacetate (129) (13.2 g; 0.1 mol) in anhydrous ether (15.0 ml). After the initial vigorous reaction had subsided the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The mixture was cooled, treated cautiously with ice (150 g) and 2M aqueous sulphuric acid (150 ml; 0.3 mol) and the resulting mixture stirred for 15 min. The ether layer was separated and the aqueous layer further extracted several times with ether. Rotary evaporation of the combined ether extracts gave an oil which was treated with 85% v/v aqueous formic acid (100 ml) and the resulting dispersion stirred and heated under reflux for 6 h.

The dispersion was cooled, poured into water (500 ml) then extracted several times with ether. The combined ether extracts were washed several times with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give the crude aldehyde which was purified as described for the individual reactions below.

(i) The brown oil obtained from 4-bromotoluene (127a) was distilled to give 2,2-di-(4-methylphenyl)acetaldehyde (133a) as a pale yellow-green oil (72%), bp 156°C/0.02 mm Hg, identified by comparison [bp, ir and ^{1}H nmr spectra and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

(ii) The orange oil obtained from 4-bromobenzotrifluoride (127b) was 2,2-di-(4-trifluoromethylphenyl)acetaldehyde (133b) (60%) identified by comparison (^{1}H nmr spectrum) with a sample prepared before, which could not be purified without decomposition.

(g) Magnesium turnings (1.4 g; 0.06 g atom) were added to a stirred solution of 4-bromo-*N,N*-dimethylaniline (127c) (4.0 g; 0.02 mol) in anhydrous tetrahydrofuran (5.0 ml) followed by ethyl bromide (3 drops). The stirred mixture refluxed spontaneously and was treated dropwise with a further solution of 4-bromo-*N,N*-dimethylaniline (127c) (8.0 g; 0.04 mol) in anhydrous ether (12.0 ml) added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool then was treated dropwise at room temperature with a solution of ethyl 2-ethoxyacetate (129) (2.6 g; 0.02 mol) in anhydrous ether (3.0 ml). After the initial vigorous exothermic reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The stirred mixture was cooled to room temperature then treated cautiously with ice (30.0 g) and 2M aqueous sulphuric acid (30.0 ml; 0.06 mol) and stirred for 15 min. The layers were separated and the aqueous layer extracted with ether. The combined ether extracts were discarded.

The aqueous layer was cooled (ice bath) and treated with 20% w/v aqueous sodium hydroxide solution until just basic, then extracted several times with ether to give a yellow-brown oil (6.2 g). This was treated with 85% v/v aqueous formic acid (20.0 ml) and the resulting blue solution stirred and heated under reflux for 6 h.

The resulting brown solution was poured into water (100 ml), extracted several times with ether and the combined ether extracts were rejected. The aqueous acidic mother liquor was stirred, cooled (ice bath) then treated portionwise with solid sodium hydrogen carbonate until just basic. Extraction with ether gave a partially crystalline green oil (3.3 g) which was triturated with ether-light petroleum (bp 40-60°C) to give the 2,2-di-(4-*N,N*-dimethylaminophenyl)-acetaldehyde (133c) as a pale green solid (0.84 g; 15%), mp 72-76°C, identical [mp, ir spectrum and tlc in hexane-dichloromethane (1:4) over silica] to a sample prepared before.

The ether-light petroleum mother liquor was rotary evaporated to give a complex green oil (2.4 g) which was flash-chromatographed over silica but gave only a series of multi-component gums (total 2.4 g) from which no identifiable material could be obtained.

(h) Grignard grade magnesium turnings (7.2 g; 0.3 g atom) were added to a stirred solution of 4-bromoanisole (127d) (18.7 g; 0.1 mol) in anhydrous tetrahydrofuran (25.0 ml) followed by ethyl bromide (3 drops). The stirred

mixture refluxed spontaneously then was treated dropwise with a further solution of 4-bromoanisole (127d) (37.4 g; 0.2 mol) anhydrous ether (60.0 ml) added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool then was treated dropwise at room temperature with a solution of ethyl 2-ethoxyacetate (129) (13.2 g; 0.1 mol) in anhydrous ether (15.0 ml). After the initial vigorous reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The mixture was cooled, treated cautiously with ice (150 g) and 2M aqueous sulphuric acid (150 ml; 0.3 mol) and stirred for 15 min. The resulting three-phase mixture was filtered to remove an intractable colourless solid (0.12 g) and the two-phase filtrate was separated. The aqueous layer was extracted several times with ether then the combined organic layers were rotary evaporated to give a yellow-brown oil (40.3 g) which was treated with 20% w/v aqueous hydrochloric acid (225 ml) and the resulting dispersion was stirred and heated under reflux for 3 h.

The mixture was allowed to cool, then was poured into water (500 ml) to give a suspension of a brown solid in an orange solution. This was filtered to give a waxy brown solid (28.7 g) which was washed with ether-light petroleum (bp 40-60°C) to give a cream solid (4.8 g) which was recrystallised from toluene-light petroleum to afford 2,2-di-(4-methoxyphenyl)acetaldehyde (133d) as a cream

solid (3.3 g; 13%), mp 106-108°C (lit,[159] 104-105°C), ν_{max} 2764 (CH=O) and 1719 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.87 (1H, d, J 2.5 Hz, CH=O), 7.15-7.08 (4H, m, ArH), 6.93-6.86 (4H, m, ArH), 4.78 (1H, d, J 2.5 Hz, CH) and 3.79 (6H, s, 2 x CH_3).

Rotary evaporation of the toluene-light petroleum and ether-light petroleum mother liquors afforded no further identifiable material.

Fluorene-9-carboxaldehyde (193)

A stirred suspension of sodium hydride (7.2 g; 0.3 mol) in anhydrous ether (60.0 ml) was treated in one portion at room temperature with a suspension of fluorene (192) (16.6 g; 0.1 mol) in anhydrous ether (40.0 ml). The stirred suspension was treated in one portion at room temperature with ethyl formate (16.3 g; 0.22 mol) then heated under reflux. A vigorous exothermic reaction occurred and heating was interrupted until this had subsided. The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 6.5 h.

The resulting brown suspension was allowed to cool to room temperature then was treated cautiously with water (175 ml). The layers were separated and the aqueous layer was washed with light petroleum (bp 40-60°C) and the combined ether-light petroleum (bp 40-60°C) extracts were discarded. The aqueous layer was stirred and cooled (ice bath) then acidified with 20% v/v aqueous sulphuric acid and the resulting emulsion extracted several times with

ether. The combined ether extracts were washed with water and with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give the known[149] aldehyde (193) as an amber oil, bp 186°C/0.17 mm Hg, which on standing crystallised to a yellow solid (17.3 g; 90%), mp 76-78°C, ν_{max} 3500-3100 br (OH), 2825 (CH=O) and 1715 and 1675 (C=O) cm^{-1}.

2-Bromo-2,2-diphenylacetaldehyde (113)

2-Bromo-2,2-diphenylacetaldehyde (113) was prepared by the reaction of 2,2-diphenylacetaldehyde (111) with bromine as described by Rowe,[137] as a pale yellow solid (yield 88%), mp 50-56°C (lit,[137] 53-56°C), ν_{max} 2725 (CH=O) and 1713 (C=O) cm^{-1}.

2-Bromo-2,2-diarylacetaldehydes (134)

A solution of the respective 2,2-diarylacetaldehyde (133) (0.05 mol) in anhydrous dichloromethane (190 ml) was stirred and treated dropwise at room temperature with a solution of bromine (12.0 g; 0.075 mol) in anhydrous dichloromethane (60.0 ml) and the resulting red-brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The red-brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (200 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave the corresponding 2-bromo-2,2-diarylacetaldehyde (134) as an oil which decomposed on

attempted distillation or flash-chromatography and was used without further purification.

(a) 2,2-Di-(4-methylphenyl)acetaldehyde (133a) afforded 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a) as a red-brown oil (100%), ν_{max} 2716 (CH=O) and 1729 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.70 (1H, s, CH=O), 7.30-7.15 (8H, m, ArH) and 2.37 (6H, s, 2 x CH_3).

(b) 2,2-Di-(4-trifluoromethylphenyl)acetaldehyde (133b) afforded 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) as a pale yellow oil (82%), ν_{max} 2835 (CH=O) and 1729 (C=O) cm^{-1}, δ_H 9.67 (1H, s, CH=O), 7.64-7.51 (4H, m, ArH) and 7.50-7.17 (4H, m, ArH).

2-Bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a)

A stirred solution of 1,1-di-(4-methylphenyl)-2-ethoxy-1-hydroxyethane (131a) (5.0 g; 0.0185 mol) in anhydrous dichloromethane (76.0 ml) was treated dropwise at room temperature with a solution of bromine (4.8 g; 0.03 mol) in anhydrous dichloromethane (24.0 ml) and the resulting red-brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The red-brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (80.0 ml), the layers were separated and the aqueous mother liquor was extracted several times with dichloromethane.

The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give the bromo-aldehyde (134a) as an amber oil (5.5 g; 98%) identified by comparison (ir and ^{1}H nmr spectra) with a sample prepared before.

The Attempted Bromination of 1,1-Di-(4-trifluoromethylphenyl)-2-ethoxy-1-hydroxyethane (131b)

A stirred solution of 1,1-di-(4-trifluoromethylphenyl)-2-ethoxy-1-hydroxyethane (131b) (3.6 g; 0.01 mol) in anhydrous dichloromethane (38.0 ml) was treated dropwise at room temperature with a solution of bromine (2.4 g; 0.015 mol) in anhydrous dichloromethane (12.0 ml) and the resulting red-brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 15 h.

The resulting brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (40.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave the unreacted alcohol (131b) as a brown oil (3.0 g; 83%) identified by comparison (^{1}H nmr spectrum) with a sample prepared before.

2-Bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (134c)

A stirred solution of 2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (133c) (1.1 g; 0.004 mol) in anhydrous dichloromethane (15.0 ml) was treated

dropwise at room temperature with a solution of bromine (0.96 g; 0.006 mol) in anhydrous dichloromethane (5.0 ml) and the resulting deep blue solution was then stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The deep blue solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (16.0 ml), the layers were separated and the aqueous mother liquor extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave an unidentified blue oil (0.34 g).

The stirred aqueous mother liquor was basified by the cautious addition of solid sodium hydrogen carbonate, then extracted several times with dichloromethane to give the bromo-aldehyde (134c) as a green oil (1.2 g; 83%), ν_{max} 2877 and 2795 (CH=O) and 1718 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.83 (1H, s, CH=O), 7.22 (4H, d, J 9.2 Hz, ArH), 6.73 (4H, d, J 9.0 Hz, ArH) and 2.97 (12H, s, 4 x CH_3), which could not be purified with decomposition.

The Attempted Bromination of 1,1-Di-(4-*N,N*-dimethylaminophenyl)-2-ethoxy-1-hydroxyethane (131c)

A stirred solution of 1,1-di-(4-*N,N*-dimethylaminophenyl)-2-ethoxy-1-hydroxyethane (131c) (1.6 g; 0.0049 mol) in anhydrous dichloromethane (19.0 ml) was treated dropwise at room temperature with a solution of bromine (1.2 g; 0.0075 mol) in anhydrous dichloromethane (6.0 ml) and the resulting blue

solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The blue solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (20.0 ml), the layers were separated and the aqueous layer extracted several times with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give a multi-component blue oil (1.9 g) from which no identifiable material could be obtained.

The Attempted Bromination of 2,2-Di-(4-methoxyphenyl)acetaldehyde (133d)

A stirred solution of 2,2-di-(4-methoxyphenyl)acetaldehyde (133d) (2.6 g; 0.01 mol) in anhydrous dichloromethane (35.0 ml) was treated dropwise at room temperature with a solution of bromine (2.4 g; 0.015 mol) in anhydrous dichloromethane (15.0 ml). On addition of the first drops of the bromine solution the colourless solution became dark brown. The dark brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The dark brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (30.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave a complex brown gum (3.1 g), trituration of which with ether gave 4,4'-dimethoxybenzophenone

(132) as a purple-grey solid (0.64g; 26%), mp 133-137°C (lit,[160] 146°C), identified by comparison (ir and ^{1}H nmr spectra) with an authentic sample.

Rotary evaporation of the ether mother liquor gave a complex brown gum (2.3 g) from which no further product was isolated.

Tetrabutylammonium Perbromide

A stirred solution of tetrabutylammonium bromide (9.7 g; 0.03 mol) and sodium bromate (1.5 g; 0.01 mol) in water (60.0 ml) was treated dropwise at room temperature with 47% w/v aqueous hydrobromic acid (7.0 ml) and the resulting yellow-orange suspension was stirred at room temperature for 10 min.

The suspension was filtered to give a yellow-orange solid (12.4 g) which was crystallised from ether-dichloromethane to give tetrabutylammonium perbromide as an orange solid (9.0 g; 62%), mp 71-74°C (lit,[141] 74-75°C).

The Attempted Reaction of 2,2-Di-(4-methoxyphenyl)acetaldehyde (133d) with Tetrabutylammonium Perbromide

A stirred solution of 2,2-di-(4-methoxyphenyl)acetaldehyde (133d) (0.64 g; 0.0025 mol) in anhydrous dichloromethane (2.5 ml) and methanol (2.5 ml) was treated dropwise at room temperature with a solution of tetrabutylammonium perbromide (1.2 g; 0.0025 mol) in anhydrous dichloromethane (5.0 ml). The resulting orange solution was then stirred at room temperature with the exclusion of atmospheric moisture for 1.5 h.

The orange solution was rotary evaporated and the residual oil was treated with water (5.0 ml) then extracted several times with dichloromethane to give a complex yellow-brown oil (1.5 g) from which no identifiable product was isolated.

The Attempted Bromination of 1,1-Di-(4-methoxyphenyl)-2-ethoxyethene (130d)

A stirred solution of 1,1-di-(4-methoxyphenyl)-2-ethoxyethene (130d) (2.8 g; 0.01 mol) in anhydrous dichloromethane (38.0 ml) was treated dropwise, at room temperature, with a solution of bromine (2.4 g; 0.015 mol) in anhydrous dichloromethane (12.0 ml) The resulting purple solution was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The purple solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (40.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give a brown gummy solid (3.0 g) which was washed with ether to give 4,4'-dimethoxybenzophenone (132) as a mauve solid (0.80 g; 33%), mp 136-140°C (lit,[160] 146°C), identified by comparison (ir and ^{1}H nmr spectra) with an authentic sample.

The ether mother liquor was rotary evaporated to give a complex brown gum (2.0 g) which yielded no identifiable material.

_N_-Bromoacetamide

_N_-Bromoacetamide was prepared by the reaction of acetamide with bromine in the presence of potassium hydroxide as described by Oliveto and Gerold,[146] as a colourless solid (yield 31%), mp 102-105°C (lit,[146] 102-105°C), ν_{max} 3131 (NH) and 1642 (C=O) cm^{-1}.

2-Bromo-1,1-diphenyl-1-hydroxyethane (147)

A stirred dispersion of 1,1-diphenylethene (146) (18.0 g; 0.1 mol) in _t_-butanol (43.0 ml) and water (17.0 ml) was cooled to 0°C (ice-salt bath) and treated dropwise over 45 min with a solution of _N_-bromoacetamide (27.6 g; 0.2 mol) in _t_-butanol (90.0 ml) and water (45.0 ml). The resulting suspension of a colourless solid in a colourless solution was stirred at 0°C for 2 h, allowed to stand under refrigeration for 15 h then stirred at 0°C for a further 2 h.

The suspension was filtered and the colourless solid (25.8 g) was treated with water (40.0 ml) and the solution extracted several times with ether to give a colourless solid (21.3 g) which was crystallised from light petroleum to give the bromohydrin (147) as a colourless microcrystalline solid (19.9 g; 72%), mp 73-74°C (lit,[144] 73°C), ν_{max} 3554 (OH) cm^{-1}.

1,1-Diphenylethene Epoxide (148)

A solution of 2-bromo-1,1-diphenyl-1-hydroxyethane (147) (13.9 g; 0.05 mol) in methanol (75.0 ml) was added dropwise at room temperature to a stirred solution of potassium hydroxide (3.4 g; 0.06 mol) in methanol (25.0 ml) and

the mixture was cooled to 0°C (ice-salt bath) and stirred at this temperature for 30 min.

The resulting colourless suspension was filtered, the colourless solid (12.0 g) was treated with water (20.0 ml) and the resulting solution extracted several times with ether to give a colourless solid which was combined with a second crop obtained by rotary evaporation of the methanol filtrate, treatment of the residue with water (20.0 ml) and extraction several times with ether to give the epoxide (148) as a colourless solid (total 8.6 g; 88%), mp 54-56°C (lit,[145] 56-57°C).

The Attempted Reaction of 1,1-Diphenylethene Epoxide (148) with Hydrogen Bromide

A solution of 1,1-diphenylethene epoxide (148) (0.78 g; 0.004 mol) in anhydrous ether (40.0 ml) was cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen bromide. The resulting yellow solution was stoppered and allowed to stand in the melting ice bath for 17 h.

The resulting yellow solution was rotary evaporated to give a multi-component yellow-brown oil (0.87 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (9:1) through dichloromethane to methanol gave only a series of multi-component gums (total 0.78 g) from which no identifiable product was isolated.

The Attempted Bromination of 2,2-Di-(2,4-dimethylphenyl)acetaldehyde (177)

A stirred solution of 2,2-di-(2,4-dimethylphenyl)acetaldehyde (177) (2.5 g; 0.01 mol) in anhydrous dichloromethane (40.0 ml) was treated dropwise at room temperature with a solution of bromine (4.0 g; 0.025 mol) in anhydrous dichloromethane (20.0 ml) and the resulting red-brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 2 h.

The red-brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (80.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave an amber oily solid (2.4 g) from which no identifiable material could be obtained.

Bromination Reactions of 2,2-Di-(naphth-1-yl)acetaldehyde (184)

(a) A stirred solution of 2,2-di-(naphth-1-yl)acetaldehyde (184) (1.2 g; 0.004 mol) in anhydrous dichloromethane (15.0 ml) was treated dropwise at room temperature with a solution of bromine (2.1 g; 0.0132 mol) in anhydrous dichloromethane (5.0 ml) and the resulting red-brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The resulting pale orange solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (35.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary

evaporation of the combined dichloromethane extracts gave a yellow foam (1.8 g) which was triturated with ether-light petroleum (bp 40-60°C) to give the dibromo derivative (187) (1.3 g; 72%) which formed colourless microcrystals, mp 167-170°C (from ethyl acetate-light petroleum), ν_{max} 1723 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.19 (1H, d, J 1.9 Hz, CH=O), 8.38-8.33 (2H, m, ArH), 7.86 (2H, dd, J 8.6 and 0.6 Hz, ArH), 7.72 (2H, d, J 7.8 Hz, ArH), 7.68-7.24 (4H, m, ArH), 7.01 (2H, d, J 7.8 Hz, ArH) and 6.32 (1H, d, J 1.6 Hz, CH), δ_C ($CDCl_3$) 198.0 (CH), 132.8 (quat), 132.5 (quat), 132.1 (quat), 129.4 (CH), 128.4 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 123.7 (quat), 123.4 (quat) and 56.0 (CH).

(b) Repetition of the reaction described in (a) before but using excess of bromine (5.2 g; 0.032 mol) gave only a complex foam (1.8 g) which yielded no identifiable material.

The Attempted Reaction of 2,2-Di-(naphth-1-yl)acetaldehyde (184) with Sulphuryl Chloride

A stirred solution of the aldehyde (184) (1.2 g; 0.004 mol) in anhydrous dichloromethane (30.0 ml) was cooled to -10°C (ice-salt bath), then treated dropwise with a solution of sulphuryl chloride (0.54 g; 0.004 mol) in anhydrous dichloromethane (10.0 ml). The resulting green solution was then stirred at -10°C with the exclusion of atmospheric moisture for 1 h.

Tlc in hexane-ether (3:2) over silica indicated that the reaction mixture contained only unreacted starting material (184) and the green solution was

therefore stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The green solution was rotary evaporated to give the unreacted aldehyde (184) as a pale green solid (1.2 g; 100%), mp 180-184°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (3:2) over silica] with a sample prepared before.

9-Bromofluorene-9-carboxaldehyde (195)

A stirred solution of fluorene-9-carboxaldehyde (193) (11.6 g; 0.06 mol) in anhydrous dichloromethane (228 ml) was treated dropwise at room temperature with a solution of bromine (14.4 g; 0.09 mol) in anhydrous dichloromethane (72.0 ml) and the resulting red-brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The red-brown solution was treated in a slow stream with 1% w/v aqueous sodium thiosulphate solution (24.0 ml), the layers were separated and the aqueous layer was extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave an orange oil (15.2 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) gave an unidentified red-brown oily solid (0.22 g).

Elution with hexane-dichloromethane (3:1) gave the bromo-aldehyde (195) (12.0 g; 73%) which formed cream microcrystals, mp 61-63°C [from ethyl acetate-light petroleum (bp 40-60°C)], ν_{max} 1724 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.45 (1H, s, CH=O), 7.72-7.62 (4H, m, ArH) and 7.51-7.34 (4H, m, ArH).

1,2-Dihydroxy-1,1-diphenylethane (143)

1,2-Dihydroxy-1,1-diphenylethane (143) was prepared by the reduction of benzilic acid (142) with lithium aluminium hydride as described by Wieland, Lewalter and Birr,[142] as a colourless solid (yield 29%), mp 124-128°C (lit,[142] 121°C), ν_{max} 3500-3100 br (OH) cm^{-1}.

The Attempted Oxidation of 1,2-Dihydroxy-1,1-diphenylethane (143) with Manganese Dioxide

(a) Activated manganese dioxide (5.0 g) was added in one portion at room temperature to a stirred solution of 1,2-dihydroxy-1,1-diphenylethane (143) (2.1 g; 0.01 mol) in anhydrous acetonitrile (50.0 ml). The resulting suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The suspension was filtered through celite and the filtrate was rotary evaporated to give a colourless solid (1.9 g), mp 108-114°C, shown by comparison [tlc in hexane-ether (2:3) over silica] with authentic samples to contain unreacted 1,2-dihydroxy-1,1-diphenylethane (143) and none of the desired 2,2-diphenyl-2-hydroxyacetaldehyde (144).

(b) Repetition of the reaction described in (a) before but at room temperature for 62 h gave only an intractable solid from which no identifiable product could be obtained.

Ethyl 2,2-Diethoxyacetate (162)

Ethyl 2,2-diethoxyacetate was prepared by the reaction of sodium ethoxide with dichloroacetic acid as described by Moffett,[147] as a colourless oil (yield 74%), bp 92°C/20 mm Hg (lit,[147] 81-83°C/12 mm Hg), ν_{max} 1755 (C=O) cm^{-1}, δ_H ($CDCl_3$) 4.86 (1H, s, CH), 4.22 (2H, q, J 7.3 Hz, CH_2), 3.72-3.56 (4H, m, 2 x CH_2) and 1.32-1.18 (9H, m, 3 x CH_3).

1,1-Diaryl-2,2-diethoxy-1-hydroxyethanes

Grignard grade magnesium turnings (6.9 g; 0.3 g atom) were added to a stirred solution of the corresponding aryl bromide (0.1 mol) in anhydrous tetrahydrofuran (25.0 ml). The mixture refluxed spontaneously and was treated dropwise with stirring with a further solution of the aryl bromide (0.2 mol) in anhydrous ether (150 ml) added at a rate sufficient to maintain reflux.

The mixture was allowed to cool then was treated dropwise with stirring at room temperature with a solution of ethyl 2,2-diethoxyacetate (162) (14.4 g; 0.1 mol) in anhydrous ether (50.0 ml). After the initial vigorous reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The mixture was cooled, treated cautiously with ice (150 g) and 2M aqueous sulphuric acid (150 ml; 0.3 mol) and stirred for 15 min. The ether layer was separated and the aqueous layer was further extracted several times with ether to give the corresponding hydroxy-acetal product which was purified by flash-chromatography as described for the individual reactions below.

(a) The oil product from reaction with bromobenzene was purified by flash-chromatography over silica.

Elution with hexane-dichloromethane (3:2) gave an unidentified pale yellow oil followed by 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) as a colourless oil (65%), bp 149°C/0.023 mm Hg, ν_{max} 3559 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.59-7.53 (4H, m, ArH), 7.36-7.20 (6H, m, ArH), 4.92 (1H, s, CH), 3.82-3.67 (2H, m, CH_2), 3.39-3.24 (3H, m, CH_2 and OH) (collapses to 2H, m on exchange with D_2O) and 1.12 (6H, t, J 7.0 Hz, 2 x CH_3).

(b) The oily product from the reaction with 4-bromoanisole (127d) was purified by flash-chromatography over silica.

Elution with hexane-ether (17:3) gave a complex pale orange oil followed by 2,2-diethoxy-1,1-di-(4-methoxyphenyl)-1-hydroxyethane (163) as a colourless oil (72%), bp 190°C/0.015 mm Hg, ν_{max} 3560-3480 (OH) cm^{-1}, δ_H ($CDCl_3$) 7.47-7.37 (4H, m, ArH), 6.85-6.79 (4H, m, ArH), 4.75 (1H, s, CH), 3.78 (6H, s, 2 x

CH_3), 3.75-3.62 (2H, m, CH_2), 3.35-3.20 (2H, m, CH_2), 3.15 (1H, s, OH) (exch) and 1.10 (6H, t, J 7.0 Hz, 2 x CH_3).

(c) The oily product from the reaction with 1-bromonaphthalene (180) was purified by flash-chromatography over silica.

Elution with hexane-ether (19:1) gave an oily colourless solid which was washed with light petroleum (bp 40-60°C) to give naphthalene as a colourless solid, mp 69-74°C (lit,[161] 80°C), identified by comparison (ir spectrum and tlc in hexane over silica) with an authentic sample.

Rotary evaporation of the light petroleum mother liquor gave 1-bromonaphthalene (180) as a colourless oil identified by comparison (ir spectrum and tlc in hexane over silica) with an authentic sample.

Elution with hexane-ether (9:1) gave a colourless solid which was combined with a second crop obtained by further elution with hexane-ether (9:1) and washing the resulting oily yellow solid with light petroleum (bp 40-60°C) to give 2,2-diethoxy-1,1-di-(naphth-1-yl)-1-hydroxyethane (188) (total 63%) which formed colourless microcrystals, mp 133-135°C (from ethyl acetate-light petroleum), ν_{max} 3485 (OH) cm^{-1}, δ_H ($CDCl_3$) 8.60-8.20 (2H, brs, ArH), 8.10-7.75 (6H, m, ArH), 7.47-7.16 (6H, m, ArH), 5.21 (1H, s, CH), 3.80-3.50 (2H, brs, CH_2), 3.67 (1H, s, OH) (exch), 3.20-2.90 (2H, brs, CH_2) and 1.10-0.90 (6H, brs, 2 x CH_3).

Rotary evaporation of the light petroleum mother liquor gave a yellow oil from which no identifiable product was isolated.

Ethyl 2,2-Di-(4-methoxyphenyl)acetate (164)

Grignard grade magnesium turnings (6.9 g; 0.3 g atom) were added to a stirred solution of 4-bromoanisole (127d) (18.7 g; 0.1 mol) in anhydrous tetrahydrofuran (25.0 ml). The stirred mixture refluxed spontaneously and was treated dropwise with a further solution of 4-bromoanisole (127d) (37.4 g; 0.2 mol) in anhydrous ether (150 ml) added at a rate sufficient to maintain reflux.

The stirred mixture was allowed to cool then was treated dropwise at room temperature with a solution of ethyl 2,2-diethoxyacetate (162) (14.4 g; 0.1 mol) in anhydrous ether (50.0 ml). After the initial vigorous exothermic reaction had subsided, the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 1h.

The stirred mixture was allowed to cool then was treated cautiously at room temperature with ice (150 g) (exothermic reaction) followed by 2M aqueous sulphuric acid (150 ml; 0.3 mol) then stirred at room temperature for 15 min.

The layers were separated, the aqueous layer was extracted several times with ether and the combined ether extracts were rotary evaporated to give a yellow oil (46.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave a series of intractable oils (total 24.5 g) followed by ethyl 2,2-di-(4-methoxyphenyl)acetate (164) as a yellow oil (10.4 g; 35%), bp 190°C/0.017 mm Hg, ν_{max} 1732 (C=O) cm^{-1}, δ_H ($CDCl_3$) 7.30-7.19 (4H, m, ArH), 6.89-6.80 (4H, m, ArH), 4.91 (1H, s, CH), 4.19 (2H, q, J 7.2 Hz, CH_2), 3.77 (6H, s, 2 x CH_3) and 1.25 (3H, t, J 7.2 Hz, CH_3).

Elution with hexane-ether (7:3) through ether to methanol gave only a series of intractable gums (total 4.6 g) from which no identifiable material could be isolated.

2,2-Di-(4-methoxyphenyl)acetic Acid (167)

The ethyl ester (164) (3.0 g; 0.01 mol) was dispersed in 2M aqueous sodium hydroxide solution (10.0 ml) and the mixture was stirred and heated under reflux for 7 h.

The mixture was cooled and extracted several times with dichloromethane to give a multi-component gum (0.63 g) which was not investigated further.

The aqueous mother liquor was cooled (ice bath) and acidified with concentrated hydrochloric acid then 2M aqueous hydrochloric acid and extracted several times with dichloromethane. The resulting three-phase mixture was filtered to remove a small amount of intractable colourless solid (0.15 g). The dichloromethane-aqueous filtrate was separated and the aqueous layer further extracted several times with dichloromethane. Rotary

evaporation of the combined dichloromethane extracts gave the carboxylic acid (167) as a colourless solid (1.5 g; 55%), mp 111-113°C (from toluene-light petroleum), ν_{max} 2734 and 2606 br (OH) and 1702 (C=O) cm^{-1}, δ_H ($CDCl_3$) 7.27-7.20 (4H, m, ArH), 6.90-6.82 (4H, m, ArH), 4.95 (1H, s, CH) and 3.78 (6H, s, 2 x CH_3).

2,2-Diaryl-2-hydroxyacetaldehydes

A solution of the corresponding 1,1-diaryl-2,2-diethoxy-1-hydroxyethane (0.05 mol) in 1,4-dioxane (250 ml) was stirred and treated with 2M aqueous hydrochloric acid (125 ml) added in one portion, and the resulting colourless solution was stirred and heated under reflux for 1 h.

The colourless solution was rotary evaporated under high vacuum (oil pump) and the oily residue treated with 10% w/v aqueous sodium hydrogen carbonate solution (125 ml) and extracted several times with ether to give the crude hydroxy-aldehyde product which was purified as described for the individual reactions below.

(a) 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) gave the known[143] 2,2-diphenyl-2-hydroxyacetaldehyde (144) as a colourless oil (88%) which was purified by bulb-to-bulb distillation to give colourless microcrystals, mp 50-53°C (bp 128°C/0.075 mm Hg), ν_{max} 3437 (OH) and 1720 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.98 (1H, d, J 1.4 Hz, CH=O) (collapses to a singlet on exchange with D_2O), 7.39-7.38 (10H, m, ArH) and 4.41 (1H, d, J 1.4 Hz, OH) (exch).

(b) The cream foam product from the reaction with 2,2-diethoxy-1,1-di-(naphth-1-yl)-1-hydroxyethane (188) was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2,2-di-(naphth-1-yl)-2-hydroxy-acetaldehyde (191) (53%) which formed colourless microcrystals, mp 155-158°C (from isopropanol), ν_{max} 3476 (OH) and 1722 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.43 (1H, d, J 0.9 Hz, CH=O) (collapses to a singlet on exchange with D_2O), 8.02-7.89 (6H, m, ArH), 7.65-7.61 (2H, m, ArH), 7.55-7.22 (6H, m, ArH) and 4.69 (1H, d, J 1.1 Hz, OH) (exch).

Further elution with hexane-ether (19:1) gave a gummy yellow solid from which no identifiable material was isolated.

Elution with hexane-ether (9:1) gave 1,2-di-(naphth-1-yl)-2-hydroxy-1-oxoethane (190) (34%) which formed cream microcrystals, mp 138-142°C [from toluene-light petroleum (80-100°C)], ν_{max} 3468 (OH) and 1673 (C=O) cm^{-1}, δ_H ($CDCl_3$) 8.74-8.69 (1H, m, ArH), 8.31 (1H, d, J 8.5 Hz, ArH), 7.88-7.21 (12H, m, ArH), 6.72 (1H, d, J 5.0 Hz, CH) (collapses to a singlet on exchange with D_2O) and 4.74 (1H, d, J 5.1 Hz, OH) (exch).

2,2-Diphenyl-2-hydroxyacetaldoxime (158)

A stirred solution of 2,2-diphenyl-2-hydroxyaldehyde (144) (1.1 g; 0.005 mol) and hydroxylamine hydrochloride (0.87 g; 0.0125 mol) in anhydrous ethanol (25.0 ml) was treated with anhydrous solid sodium carbonate (0.66 g; 0.00625

mol) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was rotary evaporated and the oily residue was treated with water (12.5 ml) to give a pale yellow solid (1.1 g) which was washed with ether-light petroleum to give the oxime (158) (0.76 g; 67%) which formed colourless microcrystals, mp 128-129°C (from toluene-light petroleum), ν_{max} 3493 and 3315 (OH) cm^{-1}, δ_H ($CDCl_3$) 8.03 (1H, s, CH), 7.47 (1H, s, OH) (exch), 7.38-7.25 (10H, m, ArH) and 3.83 (1H, s, OH) (exch).

4,4'-Dimethoxybenzoin (168)

A stirred solution of 2,2-diethoxy-1,1-di-(4-methoxyphenyl)-1-hydroxyethane (163) (0.69 g; 0.002 mol) in 1,4-dioxane (10.0 ml) was treated with 2M aqueous hydrochloric acid (5.0 ml) added in one portion and the pale yellow solution was stirred and heated under reflux for 30 min.

The resulting pale yellow solution was rotary evaporated under high vacuum (oil pump) and the oily residue was treated with water (5.0 ml) and extracted several times with ether to give a gum (0.47 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave 4,4'-dimethoxybenzoin (168) (0.35 g; 64%) which formed colourless microcrystals, mp 111-113°C (from hexane-ethyl acetate), ν_{max} 3462 (OH) and 1663 (C=O) cm^{-1}, δ_H ($CDCl_3$) 7.91-7.85 (2H, m,

ArH), 7.26-7.21 (2H, m, ArH), 6.88-6.80 (4H, m, ArH), 5.84 (1H, d, J 4.7 Hz, CH) (collapses to a singlet on exchange with D_2O), 4.52 (1H, d, J 5.8 Hz, OH) (exch), 3.81 (3H, s, CH_3) and 3.75 (3H, s, CH_3), δ_C ($CDCl_3$) 197.2 (quat), 163.8 (quat), 159.5 (quat), 131.7 (quat), 131.5 (CH), 128.9 (CH), 126.1 (quat), 114.4 (CH), 113.8 (CH), 75.1 (CH), 55.4 (CH_3) and 55.1 (CH_3).

Elution with ether to methanol gave no further identifiable material.

2,2-Di-(4-methoxyphenyl)-2-hydroxyacetaldehyde (169)

A stirred solution of 2,2-diethoxy-1,1-di-(4-methoxyphenyl)-1-hydroxyethane (163) (3.5g; 0.01 mol) in 1,4-dioxane (50.0 ml) was treated with 2M aqueous hydrochloric acid (25.0 ml) and the resulting pale yellow solution was stirred at room temperature for 24 h.

The solution was rotary evaporated under high vacuum (oil pump) and the oily residue was treated with water (25.0 ml) and extracted several times with ether to give a cream-pink gummy solid (2.6 g) trituration of which with ether-light petroleum (bp 40-60°C) gave 2,2-di-(4-methoxyphenyl)-2-hydroxyacetaldehyde (169) (2.2 g; 81%) which formed colourless needles, mp 91-93°C (from hexane), ν_{max} 3427 (OH) and 1722 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.86 (1H, d, J 1.3 Hz, CH=O) (collapses to a singlet on exchange with D_2O), 7.30-7.22 (4H, m, ArH), 6.94-6.87 (4H, m, ArH), 4.28 (1H, d, J 1.3 Hz, OH) (exch) and 3.80 (6H, s, 2 x CH_3).

The Attempted Hydrolysis of 2,2-Diethoxy-1,1-di-(naphth-1-yl)-1-hydroxy-ethane (188)

A stirred solution of the hydroxy-acetal (188) (0.77 g; 0.002 mol) in 1,4-dioxane (10.0 ml) was treated with 2M aqueous hydrochloric acid (5.0 ml) added in one portion. The colourless solution was then stirred at room temperature for 28 h during which time a colourless solid was precipitated.

Filtration of the mixture gave a colourless solid which was recrystallised from light petroleum-ethyl acetate to give the unreacted hydroxy-acetal (188) (0.50 g; 65%), mp 135-136°C, identified by comparison (mp and ir spectrum) with an authentic sample.

The aqueous 1,4-dioxane filtrate was rotary evaporated and the oily residue treated with water (5.0 ml) and extracted several times with ether to give a cream foam (0.20 g) which yielded no identifiable material.

2,2-Di-(naphth-1-yl)-2-hydroxyacetaldehyde (191)

A stirred solution of the hydroxy-acetal (188) (3.9 g; 0.01 mol) in 1,2-dimethoxyethane (50.0 ml) was treated with 2M aqueous hydrochloric acid (25.0 ml) and the resulting colourless solution was stirred and heated under reflux for 20 min.

The colourless solution was cooled then rotary evaporated and the oily residue was treated with water (25.0 ml) then extracted several times with ether. The

resulting three-phase mixture was filtered to give a solid which was combined with a second crop obtained by separating the ether-aqueous filtrate, extraction of the aqueous layer several times with ether and rotary evaporation of the combined ether extracts to give the hydroxy-aldehyde (191) as a colourless solid (total 2.8 g; 91%), mp 147-154°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (4:1) over silica] with a sample prepared before.

The Attempted Reaction of 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) with Thionyl Chloride

A stirred solution of 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) (1.4 g; 0.005 mol) in anhydrous dichloromethane (15.0 ml) was treated dropwise at room temperature with a solution of thionyl chloride (0.66 g; 0.0055 mol) in anhydrous dichloromethane (5.0 ml). Some heat was evolved and the colourless solution was stirred at room temperature with the exclusion of atmospheric moisture for 2 h.

The colourless solution was treated dropwise with 10% w/v aqueous sodium hydrogen carbonate solution (20.0 ml) and the mixture was stirred at room temperature for 5 min then the layers were separated and the aqueous layer was extracted several times with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give a colourless oil (1.4 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable gums and solids (total 0.58 g) from which no identifiable material could be obtained.

The Attempted Reaction of 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) with Phosphorus Tribromide

(a) A stirred solution of the hydroxy-acetal (152) (1.4 g; 0.005 mol) in anhydrous ether (15.0 ml) was cooled to -10°C (ice-salt bath) then treated dropwise with a solution of phosphorus tribromide (1.5 g; 0.0055 mol) in anhydrous ether (5.0 ml) at such a rate that the reaction temperature remained below 0°C. The resulting colourless solution was then stirred at room temperature with the exclusion of atmospheric moisture for 16 h.

The colourless solution was treated cautiously with 10% w/v aqueous sodium hydrogen carbonate solution (20.0 ml) and the mixture was stirred for 15 min. The layers were separated and the aqueous layer extracted several times with ether. Rotary evaporation of the combined ether extracts gave a multi-component gum (1.1 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) through dichloromethane to methanol gave only a series of complex gums (total 1.1 g) from which no identifiable product was isolated.

(b) Anhydrous dimethylformamide (8.0 ml) was stirred and cooled to 0°C (ice-salt bath) then treated dropwise with phosphorus tribromide (2.7 g; 0.01 mol). The resulting colourless suspension was allowed to warm to room temperature then was treated dropwise with a solution of the hydroxy-acetal (152) (1.4 g; 0.005 mol) in anhydrous dimethylformamide (2.0 ml). The colourless suspension was then stirred at 50°C (oil bath) with the exclusion of atmospheric moisture for 24 h.

The resulting suspension of a cream solid in a colourless solution was poured into water (50.0 ml) and extracted several times with ether. The combined ether extracts were washed with water and with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give an intractable yellow oil (0.89 g) which yielded no identifiable material.

The Attempted Reaction of 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) with Triphenylphosphine in the Presence of Carbon Tetrabromide

A solution of 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) (1.4 g; 0.005 mol) in anhydrous dichloromethane (15.0 ml) was stirred under nitrogen and cooled to 0°C (ice-salt bath) then treated in one portion with a solution of carbon tetrabromide (1.8 g; 0.0055 mol) in anhydrous dichloromethane (5.0 ml) followed by the dropwise addition of a solution of triphenylphosphine (1.4 g; 0.0055 mol) in anhydrous dichloromethane (5.0 ml). The resulting green solution was then stirred at 0°C under nitrogen for 5 h.

The green solution which became orange in contact with air was rotary evaporated and the resulting orange gum (5.3 g) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a partially crystalline yellow oil (0.52 g) from which no identifiable product could be obtained.

Further elution with hexane-ether (9:1) gave 2,2-diphenyl-2-hydroxyacetaldehyde (144) as a yellow oil (0.59 g; 56%) identified by comparison [ir spectrum and tlc in hexane-ether (7:3) over silica] with an authentic sample.

Further elution with hexane-ether (9:1) through ether to methanol gave only a series of multi-component oils (total 2.1 g) from which no identifiable product was isolated.

The Attempted Reaction of 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) with Toluene-4-sulphonyl Chloride

Toluene-4-sulphonyl chloride (1.1 g; 0.0055 mol) was added in one portion to a stirred solution of 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) (1.4 g; 0.005 mol) in Analar pyridine (5.0 ml) and the resulting solution was then stirred at room temperature with the exclusion of atmospheric moisture for 16 h.

The resulting dispersion of a colourless solid in a pink solution was poured onto ice (15.0 g), acidified with concentrated hydrochloric acid, then extracted several times with dichloromethane to give an orange-brown oil (1.6 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave an unidentified colourless oil (0.28 g).

Elution with hexane-dichloromethane (1:1) gave unreacted 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) as a yellow oil (1.1 g; 77%) identified by comparison [ir spectrum and tlc in hexane-dichloromethane (3:7) over silica] with a previously prepared sample.

The Attempted Reaction of 2,2-Diethoxy-1,1-diphenyl-1-hydroxyethane (152) with Trifluoromethanesulphonic Anhydride

A solution of trifluoromethanesulphonic anhydride (2.1 g; 0.0075 mol) in anhydrous dichloromethane (5.0 ml) was stirred and cooled to -15°C (ice-solid CO_2 bath) then treated dropwise with a solution of 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) (1.4 g; 0.005 mol) and triethylamine (1.5 g; 0.015 mol) in anhydrous dichloromethane (25.0 ml). The resulting brown solution was then stirred at -15°C for 30 min.

The brown solution was allowed to warm to room temperature, washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 13.0 ml) then

further washed with water and rotary evaporated to give a brown oil (1.9 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a series of oils (total 0.58 g) from which no identifiable product was isolated.

Elution with hexane-ether (4:1) gave unreacted 2,2-diethoxy-1,1-diphenyl-1-hydroxyethane (152) (0.73 g; 52%) as an orange oil identified by comparison [ir spectrum and tlc in hexane-ether (4:1) over silica] with an authentic sample.

Further elution with hexane-ether (3:2) through ethyl acetate to methanol gave no other identifiable material.

The Attempted Reaction of 2,2-Diphenyl-2-hydroxyacetaldehyde (144) with Thionyl Chloride

A stirred solution of 2,2-diphenyl-2-hydroxyacetaldehyde (144) (0.85 g; 0.004 mol) in anhydrous dichloromethane (12.0 ml) was treated dropwise at room temperature with a solution of thionyl chloride (0.52 g; 0.0044 mol) in anhydrous dichloromethane (4.0 ml). Heat was evolved and the solution was stirred at room temperature with the exclusion of atmospheric moisture for 1 h, after which time tlc in hexane-dichloromethane (3:7) over silica showed only the presence of the starting hydroxy-aldehyde (144). The mixture was therefore heated under reflux with the exclusion of atmospheric moisture for 4 h.

The colourless solution was rotary evaporated to give a complex pale yellow oil (0.92 g) from which no identifiable material could be obtained.

The Attempted Reaction of 2,2-Diphenyl-2-hydroxyacetaldehyde (144) with Phosphorus Tribromide

A stirred solution of 2,2-diphenyl-2-hydroxyacetaldehyde (144) (0.85 g; 0.004 mol) in anhydrous ether (12.0 ml) was cooled to -10°C (ice-salt bath) then treated dropwise with a solution of phosphorus tribromide (1.2 g; 0.0044 mol) in anhydrous ether (4.0 ml) added at such a rate that the reaction temperature remained below 0°C. The colourless solution was allowed to warm to room temperature then was stirred at room temperature with the exclusion of atmospheric moisture for 18 h.

The colourless solution was treated cautiously with 10% w/v aqueous sodium hydrogen carbonate solution (16.0 ml) then stirred for 5 min. The layers were separated and the aqueous layer was extracted several times with ether. Rotary evaporation of the combined ether extracts gave a pale yellow gum (0.76 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:1) through dichloromethane to methanol gave only a series of intractable gums and solids (total 0.73 g) from which no identifiable product was isolated.

The Attempted Reaction of 2,2-Diphenyl-2-hydroxyacetaldehyde (144) with Triphenylphosphine in the Presence of Carbon Tetrabromide

A solution of 2,2-diphenyl-2-hydroxyacetaldehyde (144) (1.1 g; 0.005 mol) in anhydrous dichloromethane (15.0 ml) was stirred under nitrogen and cooled to 0°C (ice-salt bath) then treated in one portion with a solution of carbon tetrabromide (1.8 g; 0.0055 mol) in anhydrous dichloromethane (5.0 ml) followed by the dropwise addition of a solution of triphenylphosphine (1.4 g; 0.0055 mol) in anhydrous dichloromethane (5.0 ml). The resulting yellow-brown solution was stirred at 0°C under nitrogen for 5 h.

The yellow-brown solution was rotary evaporated to give an intractable yellow gum (4.6 g) which yielded no identifiable material.

The Attempted Reaction of 2,2-Diphenyl-2-hydroxyacetaldehyde (144) with Trifluoromethanesulphonic Anhydride

A solution of trifluoromethanesulphonic anhydride (1.7 g; 0.006 mol) in anhydrous dichloromethane (4.0 ml) was stirred under nitrogen, cooled to -15°C (ice-solid CO_2 bath) then treated dropwise with a solution of the hydroxy-aldehyde (144) (0.85 g; 0.004 mol) and triethylamine (1.2 g; 0.012 mol) in anhydrous dichloromethane (20.0 ml). The resulting red-brown solution was then stirred under nitrogen in the melting ice bath for 15 h.

The solution was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 10.0 ml) then further washed with water and rotary

evaporated to give a multi-component brown oil (0.92 g) from which no identifiable material could be obtained.

The Attempted Reaction of 2,2-Diphenyl-2-hydroxyacetaldehyde (144) with Hydrogen Chloride

Calcium chloride pellets (1.1 g; 0.01 mol) were added to a stirred solution of 2,2-diphenyl-2-hydroxyacetaldehyde (144) (1.1 g; 0.005 mol) in anhydrous ether (20.0 ml) and the stirred mixture was cooled to 0°C (ice-salt bath) then saturated with anhydrous hydrogen chloride. The mixture was then stoppered and stirred in the melting ice bath for 4 h.

The resulting suspension was filtered to remove the calcium chloride pellets and the ether filtrate was dried over magnesium sulphate then rotary evaporated to give a complex pale yellow oil (1.1 g) which yielded no identifiable product.

2-Bromo-2,2-diphenylacetaldehyde (113)

Calcium chloride pellets (1.1 g; 0.01 mol) were added to a stirred solution of 2,2-diphenyl-2-hydroxyacetaldehyde (144) (1.1 g; 0.005 mol) in anhydrous ether (20.0 ml) and the stirred suspension was cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen bromide. The mixture was then stoppered and stirred in the melting ice bath for 4 h.

The mixture was filtered to remove the calcium chloride pellets, the ether filtrate was rotary evaporated and the residue treated with water (10.0 ml) then extracted several times with ether. Rotary evaporation of the combined ether extracts gave a gummy pale yellow solid (1.0 g) which was triturated with light petroleum (bp 40-60°C) to give the bromo-aldehyde (113) as a pale yellow solid (0.58 g; 42%), mp 53-57°C (lit,[137] 53-54°C), identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (3:2) over silica] with a sample prepared before.

Rotary evaporation of the light petroleum filtrate gave a multi-component yellow oil (0.42 g) from which no further product could be isolated.

The Attempted Reaction of 1,1-Di-(4-methoxyphenyl)-2,2-diethoxy-1-hydroxyethane (163) with Hydrogen Bromide

Calcium chloride (0.89 g; 0.008 mol) was finely ground then added in one portion to a stirred solution of 1,1-di-(4-methoxyphenyl)-2,2-diethoxy-1-hydroxyethane (163) (1.1 g; 0.003 mol) in anhydrous ether (30.0 ml). The stirred mixture was cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen bromide then stoppered and stirred in the melting ice bath for 4 h.

The resulting suspension of a colourless solid in an orange-brown solution was filtered. The collected solid was treated with water (10.0 ml) and extracted several times with dichloromethane to give an intractable colourless solid (0.29 g).

The ether mother liquor was rotary evaporated and the residue was treated with water (8.0 ml) then extracted several times with ether to give impure ethyl 2,2-di-(4-methoxyphenyl)acetate (164) as a red-brown oil (0.60 g) identified by comparison (ir and ^{1}H nmr spectra) with a sample prepared before.

The Attempted Reaction of 2,2-Diethoxy-1,1-di-(4-methoxyphenyl)-1-hydroxyethane (163) with Hydrogen Chloride

Calcium chloride pellets (2.2 g; 0.02 mol) were added in one portion to a stirred solution of the hydroxy-acetal (163) (3.5 g; 0.01 mol) in anhydrous ether (100 ml). The resulting mixture was then cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen chloride. The saturated mixture was stoppered and stirred in the melting ice bath for 4 h.

The mixture was then filtered to remove the calcium chloride pellets, the ether filtrate was rotary evaporated and the oily residue was treated with water (20.0 ml) then extracted several times with ether to give ethyl 2,2-di-(4-methoxyphenyl)acetate (164) as a pale brown oil (2.6 g; 87%) identified by comparison [ir spectrum and tlc in hexane-ether (3:2) over silica] with a sample prepared before.

2-Chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (170)

Calcium chloride pellets (3.3 g; 0.03 mol) were added to a stirred solution of 2,2-di-(4-methoxyphenyl)-2-hydroxyacetaldehyde (169) (4.1 g; 0.015 mol) in anhydrous ether (115 ml) and the resulting suspension was cooled to 0°C (ice-

salt bath) and saturated with anhydrous hydrogen chloride then stoppered and stirred in the melting ice bath for 4 h.

The mixture was filtered to remove the calcium chloride pellets, and the ether mother liquor was rotary evaporated and the residue treated with water (30.0 ml) then extracted several times with ether to give the chloro-aldehyde (170) as a pale brown oil (4.2 g; 96%), ν_{max} 2836 (CH=O) and 1732 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.65 (1H, s, CH=O), 7.26-7.22 (4H, m, ArH), 6.91-6.88 (4H, m, ArH) and 3.81 (6H, s, 2 x CH_3), δ_C ($CDCl_3$) 190.5 (CH), 159.7 (quat), 130.1 (CH), 129.0 (quat), 113.8 (CH), 79.6 (quat) and 55.2 (CH_3), which was used without further purification.

The Attempted Reaction of 2,2-Di-(naphth-1-yl)-2-hydroxyacetaldehyde (191) with Hydrogen Chloride

Calcium chloride pellets (0.44 g; 0.004 mol) were added to a stirred solution of 2,2-di-(naphth-1-yl)-2-hydroxyacetaldehyde (191) (0.62 g; 0.002 mol) in anhydrous ether (40.0 ml) and the mixture was cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen chloride then stoppered and stirred in the melting ice bath for 4 h.

The mixture was filtered to remove the calcium chloride pellets, the ether filtrate was rotary evaporated and the residual gum treated with water (4.0 ml) then extracted with ether (4.0 ml). The resulting three-phase mixture was filtered to give a solid which was combined with a second crop obtained by

separation of the ether-aqueous filtrate and further extraction of the aqueous layer with ether then rotary evaporation of the combined ether extracts to give a cream solid (total 0.59 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave 1,2-di-(naphth-1-yl)-1,2-dioxoethane (189) as a yellow solid (0.17 g; 27%) which formed pale yellow microcrystals, mp 192-193°C (from ethyl acetate), ν_{max} 1663 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.36 (2H, d, J 8.1 Hz, ArH) and 8.30-7.44 (12H, m, ArH).

Further elution with hexane-ether (4:1) gave 1,2-di-(naphth-1-yl)-2-hydroxy-1-oxoethane (190) as a yellow solid (0.28 g; 45%), mp 133-136°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (4:1) over silica] with a sample prepared before.

The Attempted Reaction of 2,2-Di-(naphth-1-yl)-2-hydroxyacetaldehyde (191) with Hydrogen Bromide

Calcium chloride (0.44 g; 0.004 mol) was finely ground and added in one portion to a stirred solution of 2,2-di-(naphth-1-yl)-2-hydroxyacetaldehyde (191) (0.62 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (8.0 ml). The stirred mixture was cooled to 0°C (ice-salt bath) and saturated with anhydrous hydrogen bromide then stoppered and stirred in the melting ice bath for 4 h.

The resulting yellow solution was rotary evaporated and the residue was treated with water (4.0 ml) then extracted several times with ether to give a

partially crystalline yellow oil. This was triturated with ether-light petroleum (bp 40-60°C) to give 1,2-di-(naphth-1-yl)-1,2-dioxoethane (189) as a pale yellow solid (0.08 g; 13%), mp 179-182°C, identified by comparison (mp, ir and ^{1}H nmr spectrum) with a sample prepared before.

The ether-light petroleum mother liquor was rotary evaporated and the residual yellow oil (0.77 g) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) through dichloromethane and ethyl acetate to methanol gave only a series of intractable gums and solids (total 0.50 g) from which no identifiable material could be obtained.

1,2-Naphthalenedione 1-Oxime Diarylformylmethyl Ethers

(a) Reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) with 2-bromo-2,2-diphenylacetaldehyde (113) as described by Rowe[137] gave a readily separated mixture of the *syn* oxime ether (117) as an orange solid (yield 5%), mp 153-154°C (lit,[137] 154-157°C), ν_{max} 1729 and 1645 (C=O) cm^{-1}, and the *anti* oxime ether (118) as a yellow solid (yield 57%), mp 153-154°C (lit,[137] 155-157°C), ν_{max} 1737 and 1664 (C=O) cm^{-1}.

(b) A suspension of 1,2-naphthalenedione 1-oxime lithium salt (112) (0.011 mol) in Analar acetone (80.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The resulting green suspension was stirred and treated dropwise with a solution of the corresponding 2-bromo-2,2-

diarylacetaldehyde (0.01 mol) in Analar acetone (20.0 ml) and the mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 2-15 h.

The resulting brown solution was rotary evaporated and the residue was treated with water (20.0 ml) then extracted several times with dichloromethane, with filtration to remove any unreacted lithium salt, and the combined dichloromethane extracts rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a) gave a brown gum which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:7) gave a gummy red-brown solid which was washed with light petroleum (bp 40-60°C) to give a 3:5 mixture of the *syn* and *anti* isomers of 1,2-naphthalenedione 1-oxime di-(4-methylphenyl)-formylmethyl ether (135a) (14%) which formed orange microcrystals, mp 145-147°C [from light petroleum (bp 80-100°C)], ν_{max} 1732 and 1651 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.00 (1H, s, CH=O) (*anti*), 9.91 (1H, s, CH=O) (*syn*), 8.91-8.86 (1H, m, ArH) (*anti*), 7.90-7.85 (1H, m, ArH) (*syn*), 7.53-7.16 (24H, m, ArH and CH) (*syn* and *anti*), 6.35 (1H, d, J 10.0 Hz, CH) (*anti*), 6.32 (1H, d, J 9.9 Hz, CH) (*syn*) and 2.34 (6H, s, 2 x CH_3) (*anti*) and 2.33 (6H, s, 2 x CH_3) (*syn*).

Further elution with hexane-dichloromethane (1:4) gave a red-brown solid which was washed with ether-light petroleum (bp 40-60°C) to give the pure *anti* isomer of the oxime ether (135a) (39%) which formed yellow microcrystals, mp 144-145°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 2728 (CH=O) and 1732 and 1650 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.01 (1H, s, CH=O), 8.91-8.87 (1H, m, ArH), 7.51-7.29 (8H, m, ArH), 7.19 (4H, d, J 8.1 Hz, ArH), 6.35 (1H, d, J 9.9 Hz, CH) and 2.35 (6H, s, 2 x CH_3).

(ii) The reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) with 9-bromofluorene-9-carboxaldehyde (195) gave a brown gum which was flash-chromatographed over silica.

Elution with hexane-ether (3:2) gave 1,2-naphthalenedione 1-oxime 9-formylfluoren-9-yl ether (196) (68%) which formed yellow microcrystals, mp 145-146°C (from ethanol-dimethylformamide), ν_{max} 1734 and 1662 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.68 (1H, s, CH=O), 8.19-8.14 (1H, m, ArH), 7.77-7.70 (4H, m, ArH), 7.68-7.24 (7H, m, ArH), 7.12 (1H, d, J 10.1 Hz, CH) and 6.83 (1H, d, J 10.1 Hz, CH).

(c) A suspension of the corresponding 1,2-naphthalenedione 1-oxime lithium salt (0.011 mol) in anhydrous 1,2-dimethoxyethane (80.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The resulting green or brown suspension was stirred and treated dropwise with a solution of the corresponding 2-halogeno-2,2-diarylacetaldehyde (0.01 mol) in anhydrous

1,2-dimethoxyethane (20.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 1-2 h.

The resulting brown solution was rotary evaporated and the residue treated with water (20.0 ml) then extracted several times with dichloromethane, with filtration to remove any unreacted lithium salt, and the combined dichloromethane extracts rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (170) gave unreacted 1,2-naphthalenedione 1-oxime lithium salt (112) (25%), and from the dichloromethane extracts, a brown gum which was triturated with ether and the resulting red-brown solid flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:4) gave an intractable green gum followed by a red-brown gum which was triturated with ether to give an 8:1 mixture of the *syn* and *anti* isomers of 1,2-naphthalenedione 1-oxime di-(4-methoxyphenyl)formylmethyl ether (171) (12%) which formed orange-brown microcrystals, mp 125-128°C (from isopropanol), ν_{max} 1726 and 1651 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.96 (1H, s, CH=O) (*anti*), 9.87 (1H, s, CH=O) (*syn*), 8.88-8.84 (1H, m, ArH) (*anti*), 7.91-7.86 (1H, m, ArH) (*syn*), 7.52-7.28 (16H, m, ArH and CH) (*anti* and *syn*), 6.94-6.87 (8H, m, ArH) (*anti* and *syn*), 6.34 (1H, d, J 9.9

Hz, CH) (*syn*), 6.32 (1H, d, J 9.9 Hz, CH) (*anti*), 3.80 (6H, s, 2 x CH_3) (*anti*) and 3.80 (6H, s, 2 x CH_3) (*syn*).

Elution with dichloromethane gave a tacky yellow solid which was washed with ether to give the pure *anti* isomer of the oxime ether (171) (35%) which formed yellow microcrystals, mp 128-130°C (decomp) (from isopropanol), ν_{max} 1736 and 1666 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.96 (1H, s, CH=O), 8.88-8.84 (1H, m, ArH), 7.51-7.46 (2H, m, ArH), 7.40-7.32 (6H, m, ArH), 6.94-6.86 (4H, m, ArH), 6.32 (1H, d, J 9.9 Hz, CH) and 3.80 (6H, s, 2 x CH_3).

(ii) The gummy red solid obtained from the reaction of 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198) with 2-bromo-2,2-diphenylacetaldehyde (199a) was triturated with ether-light petroleum (bp 40-60°C) to give a 1:5 mixture of the *syn* and *anti* isomers of 7-methoxy-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (201a) (81%) which formed red microcrystals, mp 136-138°C (from toluene), ν_{max} 1734 and 1665 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.07 (1H, s, CH=O) (*anti*), 9.95 (1H, s, CH=O) (*syn*), 8.50 (1H, d, J 2.6 Hz, ArH) (*anti*), 7.60-7.24 (25H, m, CH and ArH) (*anti* and *syn*), 7.01-6.95 (1H, m, ArH) (*anti*), 6.93-6.87 (1H, m, ArH) (*syn*), 6.20 (1H, d, J 9.9 Hz, CH) (*syn*), 6.17 (1H, d, J 9.9 Hz, CH) (*anti*), 3.79 (3H, s, CH_3) (*syn*) and 3.78 (3H, s, CH_3) (*anti*).

(iii) The reaction of 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198) with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (199b) gave

unreacted 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198) (28%), and from the dichloromethane extracts, a gummy red-brown solid which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave a series of intractable gums and solids (total 1.2 g) followed by 7-methoxy-1,2-naphthalenedione 1-oxime (201) as a red solid (6%), mp 117-120°C (lit,[151] 124-125°C), identified by comparison (mp and ir spectrum) with an authentic sample.

Elution with hexane-ethyl acetate (4:1) gave 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methylphenyl)formylmethyl ether (201b) (31%) which formed orange microcrystals, mp 148-151°C (decomp) (from ethanol), ν_{max} 1731 and 1660 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.01 (1H, s, CH=O), 8.53 (1H, d, J 2.6 Hz, ArH), 7.34-7.16 (10H, m, ArH), 7.00-6.96 (1H, m, ArH), 6.18 (1H, d, J 9.9 Hz, CH), 3.81 (3H, s, CH_3) and 2.34 (6H, s, 2 x CH_3).

(iv) The reaction of 7-methoxy-1,2-naphthalenedione 1-oxime lithium salt (198) with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (200c) gave unreacted lithium salt (198) (13%), and from the dichloromethane extracts, a gummy red solid which was triturated with ether and the resulting red-brown solid flash-chromatographed over silica.

Elution with hexane-ether (7:3) then (1:1) gave a 1:1 mixture of the *syn* and *anti* isomers of 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methoxy-

phenyl)formylmethyl ether (201c) (65%) which formed orange microcrystals, mp 151°C (decomp) (from hexane-1,2-dimethoxyethane), ν_{max} 2710 (CH=O) and 1735 and 1645 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.98 (1H, s, CH=O) (*anti*), 9.86 (1H, s, CH=O) (*syn*), 8.51 (1H, d, J 2.6 Hz, ArH) (*anti*), 7.51-7.20 (14H, m, ArH) (*syn* and *anti*), 6.86-6.70 (9H, m, ArH and CH) (*syn* and *anti*), 6.19 (1H, d, J 9.9 Hz, CH) (*syn*), 6.18 (1H, d, J 9.8 Hz, CH) (*anti*), 3.83 (3H, s, CH_3) (*syn*), 3.81 (3H, s, CH_3) (*anti*), 3.80 (6H, s, 2 x CH_3) (*anti*) and 3.79 (6H, s, 2 x CH_3) (*syn*).

Attempted Reaction of 2-Bromo-2,2-diphenylacetaldehyde (113) with 1,2-Naphthalenedione 1-Oxime (107)

A stirred solution of 1,2-naphthalenedione 1-oxime (107) (0.35 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (16.0 ml) was treated dropwise at room temperature with a solution of 2-bromo-2,2-diphenylacetaldehyde (113) (0.55 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (4.0 ml). The resulting brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 22 h.

The brown solution was rotary evaporated and the residual gummy brown solid (0.90 g) triturated with ether-light petroleum (bp 40-60°C) to give 1,2-naphthalenedione 1-oxime (107) as a brown solid (0.24 g; 69%), mp 97-103°C (lit,[162] 109.5°C) identified by comparison [mp, ir spectrum and tlc in hexane-ethyl acetate (1:1) over silica] with an authentic sample.

Rotary evaporation of the ether-light petroleum mother liquor gave a partially crystalline brown gum (0.58 g) shown by comparison [tlc in hexane-ethyl acetate (1:1) over silica] with authentic samples to contain only the 1,2-naphthalenedione 1-oxime (107) and 2-bromo-2,2-diphenylacetaldehyde (113) starting materials.

The Thermolysis of *Anti*-1,2-naphthalenedione 1-Oxime Diphenyl-formylmethyl Ether (118)

(a) A stirred solution of *anti*-1,2-naphthalenedione 1-oxime diphenyl-formylmethyl ether (118) (0.37 g; 0.001 mol) in anhydrous 1,2-dimethoxy-ethane (5.0 ml) was heated under reflux with the exclusion of atmospheric moisture for 4.5 h.

The resulting red-brown solution was rotary evaporated to give a red-brown oil (0.42 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:1) gave a small amount of an intractable oil followed by a mixture of the *syn* and *anti* isomers of the oxime ether (115) as an orange solid (0.06 g; 16%), mp 152-153°C, δ_C ($CDCl_3$) 196.7 (CH) (*syn*), 195.8 (CH) (*anti*), 183.4 (quat) (*anti*), 178.4 (quat) (*syn*) and 144.9-94.5 (complex pattern of signals).

Elution with hexane-dichloromethane (3:7) gave *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) as an orange brown solid (0.26 g;

70%), mp 149-151°C (lit,[137] 155-157°C), δ_C ($CDCl_3$) 195.7 (CH), 183.3 (quat), 147.0 (quat), 144.1 (CH), 136.9 (quat), 131.9 (CH), 131.4 (quat), 131.2 (CH), 130.7 (CH), 129.9 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 126.5 (quat) and 95.0 (quat).

(b) Repetition of the reaction described in (a) before but using 1,4-dioxane as solvent instead of 1,2-dimethoxyethane and with heating under reflux for 24 h gave, after work-up, a complex brown gum (0.45 g) which yielded no identifiable material.

The Photolysis of *Anti*-1,2-naphthalenedione 1-Oxime Diphenylformyl-methyl Ether (118)

A solution of *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) (0.73 g; 0.002 mol) in anhydrous 1,4-dioxane (200 ml) was water-cooled to 18°C then irradiated at 254 nm in a Hanovia photochemical reactor for 3 h.

The resulting orange solution was allowed to stand at room temperature for 2 h then was rotary evaporated to give a gummy red-orange solid (0.85 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (9:11) gave a small amount of an intractable oil followed by *syn*-1,2-naphthalenedione 1-oxime diphenylformyl-methyl ether (117) as an orange solid (0.25 g; 34%), mp 129°C (decomp) (lit,[137] 154-157°C), ν_{max} 1733 and 1648 (C=O) cm^{-1}, identified by comparison [ir

spectrum and tlc in hexane-ether (2:3) over silica] with a sample prepared before.

Elution with hexane-dichloromethane (7:13) gave *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) as a yellow solid (0.24 g; 33%), mp 129°C (decomp) (lit,[137] 155-157°C), ν_{max} 1737 and 1666 (C=O) cm^{-1}, identified by comparison (ir spectrum and tlc in hexane-ether (2:3) over silica] with a sample prepared before.

The Attempted Reaction of *Anti*-1,2-Naphthalenedione 1-Oxime Diphenylformylmethyl Ether (118) with Ethanol

A stirred solution of *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) (0.73 g; 0.002 mol) in anhydrous ethanol (20.0 ml) was heated under reflux with the exclusion of atmospheric moisture for 6 h.

The resulting brown solution was allowed to cool to room temperature and the solid which crystallised was collected and combined with a second crop obtained by rotary evaporation of the ethanol mother liquor and washing the residual brown solid with ether to give the unreacted *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) as a yellow solid (total 0.52 g; 71%), mp 147°C (decomp) (lit,[137] 155-157°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

The ether mother liquor was rotary evaporated to give a multi-component brown oil (0.14 g) which yielded no identifiable material

1,2-Naphthalenedione 1-Oxime 2-Oxopropyl Ether (136)

A stirred suspension of 1,2-naphthalenedione 1-oxime lithium salt (112) (1.0 g; 0.0055 mol) in Analar acetone (40.0 ml) was briefly heated to reflux then cooled to room temperature. The resulting green suspension was treated dropwise with stirring with a solution of 2-bromo-2,2-di-(4-trifluoromethyl-phenyl)acetaldehyde (134b) (2.1 g; 0.005 mol) in Analar acetone and the mixture stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The solution was rotary evaporated and the residue treated with water (10.0 ml) then extracted several times with dichloromethane to give a red-brown gum (2.1 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave unreacted 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) as a brown oil (1.0 g; 48%) identified by comparison [ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with a sample prepared before.

Further elution with hexane-ethyl acetate (9:1) to hexane-ethyl acetate (13:7) gave a number of intractable brown oils (total 0.87 g) from which no identifiable material could be isolated.

Elution with hexane-ethyl acetate (11:9) gave a gummy brown solid (0.27 g) which was washed with ether to afford 1,2-naphthalenedione 1-oxime 2-oxopropyl ether (136) (0.17 g; 15%) which formed yellow microcrystals, mp 110-113°C (from toluene), ν_{max} 1728 and 1658 (C=O) cm^{-1}, δ_H ($CDCl_3$) 8.79-8.74 (1H, m, ArH), 7.52-7.35 (4H, m, ArH and CH), 6.38 (1H, d, J 9.9 Hz, CH), 5.11 (2H, s, CH_2) and 2.21 (3H, s, CH_3).

The Attempted Reaction of 1,2-Naphthalenedione 1-Oxime Lithium Salt (112) with 2-Bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b)

A stirred suspension of 1,2-naphthalenedione 1-oxime lithium salt (112) (0.39 g; 0.0022 mol) in anhydrous 1,2-dimethoxyethane (16.0 ml) was briefly heated to reflux then cooled to room temperature. The green suspension was then stirred and treated dropwise at room temperature with a solution of 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) (0.82 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (4.0 ml) and the mixture stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The resulting brown solution was rotary evaporated and the residue was treated with water (4.0 ml) and extracted several times with dichloromethane to give a brown gum (1.0 g) which was flash-chromatographed over silica but gave no identifiable material.

The Attempted Acid Catalysed Reaction of 1,2-Naphthalenedione 1-Oxime (107) with 1,1-Diphenylethene Epoxide (148)

A stirred solution of 1,2-naphthalenedione 1-oxime (107) (0.87 g; 0.005 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) was treated at room temperature in one portion with a solution of 1,1-diphenylethene epoxide (148) (0.98 g; 0.005 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) followed by toluene-4-sulphonic acid monohydrate (0.01 g). The solution was then stirred at room temperature with the exclusion of atmospheric moisture for 30 min during which time tlc showed the rapid consumption of the epoxide (148).

The resulting brown solution was rotary evaporated and the residue was treated with water (20.0 ml) then extracted several times with dichloromethane to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave a series of intractable oils (total 0.45 g), followed by unreacted 1,2-naphthalenedione 1-oxime (107) as a yellow solid (0.37 g; 43%), mp 100-104°C (lit,[162] 109.5°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

Further elution with hexane-ether (9:13) through ether to methanol gave only a number of complex gums (total 0.45 g) from which no identifiable material could be obtained.

The Attempted Reaction of the Lithium Salt of 1,2-Naphthalenedione 1-Oxime (112) with 1,1-Diphenylethene Epoxide (148)

A stirred suspension of the lithium salt of 1,2-naphthalenedione 1-oxime (112) (0.98 g; 0.0055 mol) in Analar acetone (40.0 ml) was briefly heated to reflux then cooled to room temperature. The green suspension was then stirred and treated dropwise with a solution of 1,1-diphenylethene epoxide (148) (0.98 g; 0.005 mol) in Analar acetone (10.0 ml) and the mixture stirred at room temperature with the exclusion of atmospheric moisture for 69 h.

The green suspension was filtered to give a green solid which was combined with a further crop of green solid obtained by rotary evaporation of the acetone filtrate followed by trituration of the residue with ether to give the unreacted lithium salt (112) (total 0.89 g; 91%), mp 252°C (decomp with gas evolution) (lit,[137] 263-267°C), identified by comparison [mp, ir spectrum and tlc in hexane ether (1:1) over silica] with a sample prepared before.

Rotary evaporation of the ether mother liquor gave the unreacted epoxide (148) as a brown solid (0.90 g; 92%), mp 54-56°C (lit,[145] 56-57°C), identified by comparison [mp, ir spectrum and tlc in hexane ether (1:1) over silica] with a sample prepared before.

The Attempted Acid Catalysed Reaction of 2,2-Diphenyl-2-hydroxy-acetaldoxime (158) with 2-Naphthol (157)

A stirred solution of 2,2-diphenyl-2-hydroxyacetaldoxime (158) (1.1 g; 0.005 mol) in anhydrous toluene (35.0 ml) was treated at room temperature with a solution of 2-naphthol (157) (0.72 g; 0.005 mol) in anhydrous toluene (15.0 ml) added in one portion, followed by toluene-4-sulphonic acid monohydrate (0.095 g). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of any water formed (Dean and Stark apparatus) for 1 h.

The resulting brown solution was washed twice with 10% aqueous sodium hydrogen carbonate solution (2 x 5.0 ml) then rotary evaporated to give a gummy brown solid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane to hexane-ether (19:1) gave only a series of intractable gums and solids (total 0.58 g) from which no identifiable product could be obtained, followed by 2-naphthol (157) as a cream solid (0.28 g; 38%), mp 113-116°C (lit,[163] 122-123°C), identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

The Thermolysis of 1,2-Naphthalenedione 1-Oxime 9-Formylfluoren-9-yl Ether (196)

A suspension of 1,2-naphthalenedione 1-oxime 9-formylfluoren-9-yl ether (196) (1.5 g; 0.004 mol) in Analar methanol (40.0 ml) was stirred and heated under reflux with the exclusion of atmospheric moisture for 21 h.

The resulting red-brown solution was rotary evaporated to give a red-brown foam (1.3 g) which was triturated with light petroleum (bp 40-60°C) to afford an oxime ether isomeric with the starting material (196) (1.1 g; 73%) which formed yellow-orange microcrystals, mp 154-156°C (from ethyl acetate-light petroleum), ν_{max} 1731 and 1660 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.67 (1H, s, CH=O), 8.67-8.62 (1H, m, ArH), 7.82-7.68 (4H, m, ArH), 7.59-7.25 (8H, m, ArH) and 6.37 (1H, d, J 9.9 Hz, CH).

The Attempted Reaction of the Presumed 6-Methoxy-1,2-naphthalenedione 1-Oxime Lithium Salt (212) with 2-Bromo-2,2-diphenyl-acetaldehyde (113)

A suspension of the presumed 6-methoxy-1,2-naphthalenedione 1-oxime lithium salt (212) (0.92 g; 0.0044 mol) in anhydrous 1,2-dimethoxyethane (32.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The stirred suspension was treated dropwise at room temperature with a solution of 2-bromo-2,2-diphenylacetaldehyde (113) (1.1 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (8.0 ml) and the brown suspension was stirred at room temperature with the exclusion of atmospheric moisture for 68 h.

The resulting brown solution was rotary evaporated and the residual brown gum was treated with water (30.0 ml) then extracted several times with dichloromethane then with ethyl acetate. The combined organic extracts were rotary evaporated to give a complex brown gum (1.2 g) from which no identifiable material could be obtained.

3,3-Diaryl-3*H*-naphth[2,1-*b*]-1,4-oxazines

(a) 3,3-Diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116) was prepared by heating *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) with triphenylphosphine in anhydrous 1,2-dimethoxyethane as described by Rowe,[137] as a pink solid (yield 50%), mp 120-126°C (lit,[137] 124-125°C).

(b) A solution of the corresponding 1,2-naphthalenedione 1-oxime diarylformylmethyl ether (0.004 mol) in anhydrous tetrahydrofuran (20.0 ml) was stirred and treated at room temperature with a solution of triphenylphosphine (2.1 g; 0.008 mol) in anhydrous tetrahydrofuran (20.0 ml) added in one portion. The resulting yellow solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 21 h.

The resulting brown solution was rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The gummy brown solid obtained from the reaction of *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (11:9) gave a waxy orange solid which was washed with light petroleum (bp 40-60°C) to give 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116) as an orange solid (69%), mp 118-125°C (lit,[137] 124-125°C), which was identified by comparison (mp and ir spectrum) with a sample prepared before and was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

Elution with dichloromethane gave an orange oil which was triturated with ethyl acetate to give *syn*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (117) as an orange solid (3%), mp 147°C (decomp) (lit,[137] 154-157°C), identified by comparison [ir spectrum and tlc in hexane-ether (2:3) over silica] with a sample prepared before.

(ii) The brown gum obtained from the reaction of 1,2-naphthalenedione 1-oxime 9-formylfluoren-9-yl ether (196) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3,3-spirofluoren-9-yl-3*H*-naphth[2,1-*b*]-1,4-oxazine (197) (12%) which formed cream microcrystals, mp 172-174°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1627 (C=N) cm^{-1}, δ_H ($CDCl_3$)

8.63-8.58 (1H, m, ArH), 7.85-7.22 (13H, m, ArH and CH) and 7.13 (1H, d, J 8.8 Hz, ArH), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

(c) Repetition of the reaction described in (b) before but using 1,2-dimethoxyethane as the solvent and with heating under reflux for 15 h gave, after rotary evaporation, the crude product which was purified as described for the individual reactions below.

(i) The gummy red-brown solid obtained from the reaction of the *anti* isomer of 1,2-naphthalenedione 1-oxime di-(4-methylphenyl)formylmethyl ether (135a) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) gave 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a) (73%) which formed tan microcrystals, mp 157-159°C [from light petroleum (bp 80-100°C)], δ_H ($CDCl_3$) 8.50-8.46 (1H, m, ArH), 8.01 (1H, s, CH), 7.73-7.64 (2H, m, ArH), 7.56-7.50 (1H, m, ArH), 7.39-7.31 (5H, m, ArH), 7.20-7.13 (5H, m, ArH) and 2.32 (6H, s, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a red-brown spot which faded on removal of the irradiation source.

(ii) The deep red gum obtained from the reaction of the *anti* isomer of 1,2-naphthalenedione 1-oxime di-(4-methoxyphenyl)formylmethyl ether (171) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a solid which was recrystallised from ethyl acetate to give 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172) (62%) which formed colourless microcrystals, mp 164-165°C (from ethyl acetate), δ_H ($CDCl_3$) 8.49-8.44 (1H, m, ArH), 7.96 (1H, s, CH), 7.73-7.63 (3H, m, ArH), 7.56-7.46 (1H, m, ArH), 7.46-7.26 (4H, m, ArH), 7.15 (1H, d, J 8.8 Hz, ArH), 6.89-6.82 (4H, m, ArH) and 3.77 (6H, s, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a purple-red spot which faded on removal of the irradiation source.

(iii) The brown gum obtained from the reaction of a 1:5 mixture of the *syn* and *anti* isomers of 7-methoxy-1,2-naphthalenedione 1-oxime diphenylformyl-methyl ether (201a) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3,3-diphenyl-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202a) (91%) which formed colourless microcrystals, mp 149-150°C (from ethanol), ν_{max} 1623 (C=N) cm^{-1}, δ_H ($CDCl_3$) 8.01 (1H, s, CH), 7.77 (1H, d, J 2.6 Hz, ArH), 7.62-7.56 (2H, m, ArH), 7.48-7.25 (10H, m, ArH), 7.05-6.98 (2H, m, ArH) and 3.96 (3H, s, CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

(iv) The gummy brown solid obtained from the reaction of the *anti* isomer of 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methylphenyl)formylmethyl ether (201b) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3,3-di-(4-methylphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202b) (62%) which formed cream microcrystals, mp 182-184°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1626 (C=N) cm^{-1}, δ_H ($CDCl_3$) 7.99 (1H, s, CH), 7.77 (1H, d, J 2.6 Hz, ArH), 7.62-7.55 (2H, m, ArH), 7.36-7.25 (4H, m, ArH), 7.17-7.11 (4H, m, ArH), 7.04-6.98 (2H, m, ArH), 3.92 (3H, s, CH_3) and 2.32 (6H, s, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

(v) The red-brown gum obtained from the reaction of a 1:1 mixture of the *syn* and *anti* isomers of 7-methoxy-1,2-naphthalenedione 1-oxime di-(4-methoxyphenyl)formylmethyl ether (201c) was flash-chromatographed over silica.

Elution with hexane-ether (7:3) gave unreacted triphenylphosphine as a beige solid (0.19 g), mp 79-80°C (lit,[164] 80°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (2:3) over silica] with an authentic sample.

Further elution with hexane-ether (7:3) gave 3,3-di-(4-methoxyphenyl)-9-methoxy-3*H*-naphth[2,1-*b*]-1,4-oxazine (202c) (85%) which formed pale pink microcrystals, mp 142-143°C (from isopropanol), ν_{max} 1625 (C=N) cm^{-1}, δ_H ($CDCl_3$) 7.94 (1H, s, CH), 7.77 (1H, d, J 2.6 Hz, ArH), 7.61-7.55 (2H, m, ArH), 7.37-7.31 (4H, m, ArH), 7.02-6.97 (2H, m, ArH), 6.89-6.83 (4H, m, ArH), 3.97 (3H, s, CH_3) and 3.77 (6H, s, 2 x CH_3), which was photochromic on a silica tlc

plate, irradiation at 254 nm giving a purple-brown spot which faded on removal of the irradiation source.

(d) A suspension of the corresponding 1,2-naphthalenedione 1-oxime lithium salt (0.0044 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The resulting green suspension was stirred and treated dropwise at room temperature with a solution of the respective 2-halogeno-2,2-diarylacetaldehyde (0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The resulting suspension of a green solid in a brown solution was treated with a solution of triphenylphosphine (2.1 g; 0.008 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) added in one portion and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 15-21 h.

The resulting mixture was cooled and filtered to remove some insoluble solid and the filtrate was rotary evaporated. The residue was treated with water (8.0 ml) then extracted several times with dichloromethane and the combined extracts rotary evaporated to obtain the crude product which was purified as described for the individual reactions below.

(i) The purple gum obtained from the reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) and 2-bromo-2,2-diphenylacetaldehyde (113) was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave impure triphenylphosphine (0.14 g) as a gummy purple solid, identified by comparison [ir spectrum and tlc in hexane-ether (7:3) over silica] with an authentic sample.

Further elution with hexane-ether (4:1) gave a gummy brown solid which was washed with light petroleum (bp 40-60°C) to give 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine (116) as a yellow solid (41%), mp 121-124°C (lit,[137] 124-125°C), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source and was identified by comparison [mp, ir spectrum and tlc in hexane-ether (7:3) over silica] with an authentic sample.

(ii) The brown gum obtained from the reaction of 1,2-naphthalenedione 1-oxime lithium salt (112) and 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (170) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted triphenylphosphine as a pale blue-green solid (0.14 g), mp 79-81°C (lit,[164] 80°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (9:1) gave a cream solid which was combined with a second crop obtained by further elution with hexane-ether (9:1) and washing the resulting deep red solid with ether-light petroleum (bp 40-60°C) to give 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (172) as a cream solid (total 68%), mp 164-166°C, which was photochromic on a silica tlc plate, irradiation at 254 nm giving a purple-red spot which faded on removal of the irradiation source and was identified by comparison [mp, ir spectrum and tlc in hexane-ether (3:2) over silica] with a sample prepared before.

(e) A solution of 1,2-naphthalenedione 1-oxime 9-formylfluoren-9-yl (196) (0.73 g; 0.002 mol) in anhydrous 1,4-dioxane (10.0 ml) was stirred and treated at room temperature with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,4-dioxane (10.0 ml) added in one portion. The resulting solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 30 min.

The resulting brown solution was rotary evaporated to give a brown gum (2.0 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (13:7) gave 3,3-spirofluoren-9-yl-3*H*-naphth[2,1-*b*]-1,4-oxazine (197) as a pale orange-brown solid (0.18 g; 27%), mp 161-165°C, which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source, and was identified by comparison (ir spectrum) with a sample prepared before.

Attempted Reaction of *Anti*-1,2-naphthalenedione 1-Oxime Diphenylformylmethyl Ether (118) with Triethyl Phosphite

A solution of *anti*-1,2-naphthalenedione 1-oxime diphenylformylmethyl ether (118) (0.73 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was stirred and treated at room temperature with a solution of triethyl phosphite (0.66 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) added in one portion. The resulting solution was then stirred and treated under reflux with the exclusion of atmospheric moisture for 18 h.

The resulting red solution was rotary evaporated and the residue was treated with water (5.0 ml) and extracted several times with dichloromethane to give a red oil (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave impure benzophenone (277) as an orange-brown solid (0.06 g; 16%), mp 42-44°C (lit,[165] 49°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (3:2) over silica] with an authentic sample.

Elution with hexane-ether (19:1) through ether and ethyl acetate to methanol gave only a series of intractable oils (total 0.83 g) from which no identifiable product was obtained.

1,2-Dihydro-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (139)

A solution of 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a) (0.73 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was stirred and treated dropwise at room temperature over 15 min with a solution of sodium borohydride (0.38 g; 0.01 mol) in water (5.0 ml). The resulting pink suspension was then stirred at room temperature for 21 h.

The pink suspension was rotary evaporated and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane to give the dihydronaphthoxazine derivative (139) (0.69 g; 95%) which formed cream microcrystals, mp 175-178°C [from light petroleum (bp 80-100°C)], ν_{max} 3408 (NH) cm^{-1}, δ_H ($CDCl_3$) 7.76-7.70 (2H, m, ArH), 7.44-7.27 (8H, m, ArH), 7.13 (4H, d, J 8.0 Hz, ArH), 3.95 (2H, s, CH_2), 3.70-3.20 (1H, brs, NH) (exch) and 2.30 (6H, s, 2 x CH_3).

The Oxidation of 1,2-Dihydro-3,3-di-(4-methylphenyl)-3H-naphth[2,1-*b*]-1,4-oxazine (139) with Manganese Dioxide to give 3,3-Di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a)

Activated manganese dioxide (0.50 g) was added in one portion at room temperature to a stirred solution of 1,2-dihydro-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (139) (0.36 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 15 h.

The suspension was filtered through celite and the filtrate was rotary evaporated to give a red-brown gum (0.32 g) which was triturated with light petroleum (bp 40-60°C). The insoluble beige solid (0.22 g) was collected then flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave a red gummy solid (0.04 g) which was washed with ether-light petroleum (bp 40-60°C) to give 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a) as a pink solid (0.02 g; 6%), mp 157-159°C, identified by comparison [mp and tlc in hexane-ether (7:3) over silica] with a sample prepared before.

Further elution with hexane-ether (19:1) through to methanol gave only a series of intractable solids (total 0.18 g) from which no identifiable material could be obtained.

2-Cyano-1,2-dihydro-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (140)

A solution of 3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (137a) (0.73 g; 0.002 mol) in glacial acetic acid (5.0 ml) was stirred and treated at room temperature with potassium cyanide (0.65 g; 0.01 mol), added in one portion. The resulting mixture was then stirred and heated at 100°C for 6 h.

The resulting brown suspension was allowed to cool then rotary evaporated under high vacuum (oil pump) and the residue was treated with water (10.0 ml)

then extracted several times with dichloromethane. The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give the cyanodihydronaphthoxazine derivative (140) (0.63 g; 81%) which formed colourless microcrystals, mp 244-245°C (from toluene), ν_{max} 3404 (NH), 2238 (C≡N) and 1630 (NH def) cm^{-1}, δ_H ($CDCl_3$) 7.77-7.01 (14H, m, ArH), 5.35 (1H, d, J 4.3 Hz, CH), 4.66 (1H, d, J 4.7 Hz, NH) (exch), 2.33 (3H, s, CH_3) and 2.20 (3H, s, CH_3).

2-Cyano-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (141)

A solution of 2-cyano-1,2-dihydro-3,3-di-(4-methylphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine (140) in anhydrous 1,2-dimethoxyethane (10.0 ml) was stirred and treated at room temperature with activated manganese dioxide (0.50 g) added in one portion. The resulting mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 16 h.

The suspension was filtered through celite and the filtrate was rotary evaporated to give the cyanonaphthoxazine derivative (141) (0.39 g; 100%) which formed orange microcrystals, mp 224-225°C [from light petroleum (bp 80-100°C)], ν_{max} 2217 (C≡N) cm^{-1}.

The Attempted Reaction of 1,2-Naphthalenedione 1-Oxime 9-Formylfluoren-9-yl Ether (195) with Triphenylphosphine in 1,2-Dimethoxyethane

A suspension of the oxime ether (195) (0.73 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (30.0 ml) was stirred and treated at room temperature with a solution of triphenylphosphine (1.0 g; 0.004 mol) in 1,2-dimethoxyethane (10.0 ml) added in one portion. The resulting suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 h.

The resulting brown solution was rotary evaporated and the residual red-brown gum (1.8 g) flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) through dichloromethane to methanol gave only a series of intractable gums and solids (total 1.7 g) from which no product could be identified.

1,2-Naphthalenedione 2-Oxime Lithium Salt (121)

A solution of 1,2-naphthalenedione 2-oxime (69.2 g; 0.4 mol) (120) in Analar acetone (1400 ml) was stirred and treated dropwise at room temperature with a solution of lithium hydroxide monohydrate (16.8 g; 0.4 mol) in water (200 ml). The resulting brown solution was then stirred at room temperature for 30 min.

The brown solution was rotary evaporated and the brown solid residue was slurried with ethyl acetate and briefly heated to reflux then hot filtered to give

the lithium salt (121) as a russet solid (71.6 g; 100%), mp 190°C (decomp) (lit,[137] 205-209°C), ν_{max} 1612 (C=N) cm^{-1}, which was used without further purification.

1,2-Naphthalenedione 2-Oxime Diarylformylmethyl Ethers

(a) *Anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) was prepared by the reaction of 1,2-naphthalenedione 2-oxime lithium salt (121) with 2-bromo-2,2-diphenylacetaldehyde (113) as described by Rowe,[137] as a yellow solid (yield 78%), mp 165-168°C (lit,[137] 170-173°C), ν_{max} 1726 and 1662 (C=O) cm^{-1}.

(b) A suspension of 1,2-naphthalenedione 2-oxime lithium salt (121) (5.9 g; 0.033 mol) in Analar acetone (240 ml) was stirred and briefly heated to reflux then cooled to room temperature. The resulting suspension was stirred and treated dropwise at room temperature with a solution of the corresponding 2-halogeno-2,2-diarylacetaldehyde (0.03 mol) in Analar acetone (60.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 h.

The resulting brown solution was rotary evaporated and the residual brown gum was treated with water and extracted several times with dichloromethane to give the crude product which was purified as described for the individual reactions below.

(i) The gummy brown solid obtained from the reaction of the lithium salt (121) with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (134a) was triturated with ether to afford 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) (62%) which formed yellow microcrystals, mp 177-180°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1732 and 1678 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.97 (1H, s, CH=O), 8.13-8.09 (1H, m, ArH), 7.61-7.54 (1H, m, ArH), 7.45-7.38 (1H, m, ArH), 7.33-7.15 (10H, m, ArH), 6.91 (1H, d, J 10.5 Hz, CH) and 2.34 (6H, s, 2 x CH_3).

(ii) The brown gum obtained from the reaction of the lithium salt (121) with 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) was flash-chromatographed over silica.

Elution with hexane-ether (3:1) gave 1,2-naphthalenedione 2-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (216b) (32%) which formed yellow microcrystals, mp 184-185°C (from toluene), ν_{max} 1733 and 1679 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.02 (1H, s, CH=O), 8.13-8.09 (1H, m, ArH), 7.71-7.25 (12H, m, ArH and CH) and 7.00 (1H, d, J 10.0 Hz, CH).

(iii) The reaction of the lithium salt (121) with 9-bromofluorene-9-carboxaldehyde (195) gave 1,2-naphthalenedione 2-oxime 9-formylfluoren-9-yl ether (223) (67%) which formed yellow microcrystals, mp 176-184°C (decomp) (from ethanol-dimethylformamide), ν_{max} 1733 and 1672 (C=O) cm^{-1}, δ_H ($CDCl_3$)

9.67 (1H, s, CH=O), 8.19-8.14 (1H, m, ArH), 7.76-7.70 (4H, m, ArH), 7.62-7.25 (7H, m, ArH), 7.19 (1H, d, J 10.1 Hz, CH) and 6.83 (1H, d, J 10.0 Hz, CH).

(c) Repetition of the reaction described in (b) before but in anhydrous 1,2-dimethoxyethane at room temperature for 1 h gave, after work-up, the crude product which was purified as described for the individual reactions below.

(i) The gummy brown solid obtained from the reaction of the lithium salt (121) with 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (134b) was washed with ether to give 1,2-naphthalenedione 2-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (216a) (44%) as yellow microcrystals, mp 182°C (decomp with gas evolution), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(ii) The gummy brown solid obtained from the reaction of the lithium salt (121) with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (215d) was flash-chromatographed over silica.

Elution with dichloromethane gave a gummy yellow-brown solid which was washed with ether to afford 1,2-naphthalenedione 2-oxime di-(4-methoxyphenyl)formylmethyl ether (216d) (44%) which formed yellow microcrystals, mp 165-166°C (from ethyl acetate-hexane), ν_{max} 1739 and 1673 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.93 (1H, s, CH=O), 8.14-8.09 (1H, m, ArH), 7.61-7.53

(1H, m, ArH), 7.46-7.23 (8H, m, ArH), 6.93-6.85 (4H, m, ArH) and 3.79 (6H, s, 2 x CH_3).

The Attempted Reaction of 1,2-Naphthalenedione 2-Oxime Lithium Salt (121) with 2-Bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (134c)

A suspension of 1,2-naphthalenedione 2-oxime lithium salt (121) (1.0 g; 0.0055 mol) in Analar acetone (40.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The stirred suspension was then treated dropwise at room temperature with a solution of 2-bromo-2,2-di-(4-*N,N*-dimethylaminophenyl)acetaldehyde (134c) (1.8 g; 0.005 mol) in Analar acetone (10.0 ml), and the mixture stirred at room temperature with the exclusion of atmospheric moisture for 5 h.

The resulting brown solution was rotary evaporated and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane to give a brown gum (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) through ether to methanol gave only a series of intractable gums and solids (total 1.2 g) from which no identifiable material could be obtained.

The aqueous mother liquor was acidified with 2M aqueous hydrochloric acid then extracted several times with dichloromethane to give 1,2-

naphthalenedione 2-oxime (120) as a brown solid (0.22 g; 23%), mp 134-135°C (lit,[162] 162-164°C), identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

2,2-Diaryl-2*H*-naphth[1,2-*b*]-1,4-oxazines

(a) 2,2-Diphenyl-2*H*-naphth[1,2-*b*]-1,4-oxazine (123) was prepared by the reaction of *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) with triphenylphosphine as described by Rowe,[137] as a green solid (yield 35%), mp 112-116°C (lit,[137] 115-124°C).

(b) A solution of the corresponding 1,2-naphthalenedione 2-oxime diarylformylmethyl ether (0.02 mol) in anhydrous 1,2-dimethoxyethane (150 ml) was stirred and treated in one portion at room temperature with a solution of triphenylphosphine (10.5 g; 0.04 mol) in anhydrous 1,2-dimethoxyethane (100 ml). The resulting solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 15-17 h.

The resulting brown solution was rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The brown gum obtained from the reaction of 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) gave unreacted triphenylphosphine as a beige solid (2.9 g), mp 80-81°C (lit,[164] 80°C), identified by comparison [mp and tlc in hexane-dichloromethane (1:1) over silica with an authentic sample.

Elution with dichloromethane gave a gummy dark green solid which was washed with ether to give 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) (41%) as cream microcrystals, mp 173-176°C (from ethyl acetate), δ_H ($CDCl_3$) 8.34-8.29 (1H, m, ArH), 7.96 (1H, s, CH), 7.76-7.71 (1H, m, ArH), 7.52-7.33 (8H, m, ArH), 7.16-7.12 (4H, m, ArH) and 2.31 (6H, s, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a red spot which faded on removal of the irradiation source.

(ii) The brown gum obtained from the reaction of 1,2-naphthalenedione 2-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (216b) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted triphenylphosphine as a cream solid (0.62 g), mp 74-82°C (lit,[164] 80°C), identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (17:3) gave a purple gum which was triturated with ether-light petroleum (bp 40-60°C) to give 2,2-di-(4-trifluoromethylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218b) as a grey-green solid (0.6%), mp 100°C (decomp).

Further elution with hexane-ether (3:1) through ether to methanol gave no further identifiable material.

(iii) The gummy brown solid obtained from the reaction of 1,2-naphthalenedione 2-oxime di-(4-methoxyphenyl)formylmethyl ether (216d) was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave a green solid which was dissolved in dichloromethane and clarified with animal charcoal to give 2,2-di-(4-methoxyphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218d) (52%) which formed pale pink microcrystals, mp 133-134°C (from isopropanol), δ_H ($CDCl_3$) 8.31-8.26 (1H, m, ArH), 7.91 (1H, s, CH), 7.76-7.70 (1H, m, ArH), 7.50-7.33 (8H, m, ArH), 6.89-6.81 (4H, m, ArH) and 3.76 (6H, s, 2 x CH_3).

(iv) The brown gum obtained from the reaction of 1,2-naphthalenedione 2-oxime 9-formylfluoren-9-yl ether (223) was flash-chromatographed over silica. Elution with hexane-dichloromethane (7:3) gave unreacted triphenylphosphine as a beige solid (0.30 g), mp 76-81°C (lit,[164] 80°C), identified by comparison [mp and tlc in hexane-dichloromethane (1:4) over silica] with an authentic sample.

Elution with hexane-dichloromethane (3:7) gave impure 2,2-spirofluoren-9-yl-2*H*-naphth[1,2-*b*]-1,4-oxazine (224) as a red oil (6%) which could not be further purified without decomposition. The crude naphthoxazine derivative (224) was

photochromic on a silica tlc plate, irradiation at 254 nm giving a red spot which faded on removal of the irradiation source.

2,2-Di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a)

A stirred solution of 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)-formylmethyl ether (216a) (0.79 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated in one portion, at room temperature, with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous ethanol (5.0 ml). The solution was stirred with the exclusion of atmospheric moisture and heated under reflux for 7.5 h.

The resulting brown solution was rotary evaporated and the residual brown gum (1.8 g) flash-chromatographed over silica.

Elution with hexane-dichloromethane (2:3) gave a complex green oil (0.46 g) from which no identifiable product was isolated.

Elution with hexane-dichloromethane (1:1) gave the naphthoxazine derivative (218a) as a green solid (0.21 g; 29%), mp 160-168°C, identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:4) over silica] with a previously prepared sample.

Elution with hexane-dichloromethane (3:7) to dichloromethane gave a multi-component purple oil (0.21 g) from which no identifiable material could be obtained.

3,4-Dihydro-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (220)

A solution of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) (0.73 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was stirred and treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.38 g; 0.01 mol) in water (5.0 ml). The resulting beige suspension was then stirred at room temperature for 5 h.

The suspension was rotary evaporated and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give a purple solid (0.50 g). This was washed with ether to give the dihydronaphthoxazine derivative (220) (0.34 g; 47%) which formed colourless microcrystals, mp 205-206°C (from ethyl acetate-light petroleum), ν_{max} 3388 (NH) and 1634 (NH def) cm^{-1}, δ_H ($CDCl_3$) 8.00-6.50 (9H, brs, ArH, CH_2 and NH), 7.37 (4H, d, J 8.3 Hz, ArH), 7.09 (4H, d, J 8.3 Hz, ArH) and 2.28 (6H, s, 2 x CH_3), on D_2O shake becomes 8.34 (1H, d, J 8.6 Hz, ArH), 7.67 (1H, d, J 7.8 Hz, ArH), 7.54-7.00 (11H, m, ArH), 6.81 (1H, d, J 8.7 Hz, ArH), 3.88 (2H, s, CH_2) and 2.28 (6H, s, 2 x CH_3).

The Oxidation of 3,4-Dihydro-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (220) with Manganese Dioxide to give 2,2-Di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a)

A solution of 3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (220) (0.09 g; 0.00025 mol) in anhydrous acetonitrile (5.0 ml) was stirred and treated with activated manganese dioxide (0.13 g) added in one portion. The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a colourless glass (0.06 g) which was triturated with ether-light petroleum (bp 40-60°C) to give 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) as a grey solid (0.03 g; 33%), mp 174-179°C, m/z (EIMS) 363 (M^+), identified by comparison [mp and tlc in hexane-dichloromethane (2:3) over silica] with a sample prepared before.

Rotary evaporation of the ether-light petroleum mother liquor gave a complex brown gum (0.03 g) from which no identifiable product could be obtained.

3-Cyano-3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (221)

A solution of 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) (0.73 g; 0.002 mol) in glacial acetic acid (5.0 ml) was stirred and treated at

room temperature with potassium cyanide (0.65 g; 0.01 mol) added in one portion. The resulting mixture was then stirred at 100°C for 6 h.

The red-brown suspension was rotary evaporated under high vacuum (oil pump) and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane. The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution, then rotary evaporated to give a brown foam (0.67 g) which was triturated with ether to give the cyanodihydronaphthoxazine derivative (221) (0.42 g; 54%) which formed colourless microcrystals, mp 225-228°C [from light petroleum (bp 80-100°C)], ν_{max} 3405 (NH) and 1640 (NH def) cm^{-1}, δ_H ($CDCl_3$) 8.43-8.39 (1H, m, ArH), 7.73-7.69 (1H, m, ArH), 7.61-7.19 (10H, m, ArH), 7.03-6.98 (1H, m, ArH), 6.79 (1H, d, J 8.7 Hz, ArH), 5.28 (1H, s, CH), 4.42 (1H, brs, NH) (exch), 2.34 (3H, s, CH_3) and 2.19 (3H, s, CH_3).

3-Cyano-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (222)

A solution of 3-cyano-3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (221) (0.39 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was stirred and treated at room temperature with activated manganese dioxide (0.50 g) added in one portion. The suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 19 h.

The suspension was filtered through celite and the filtrate was rotary evaporated to give the cyanonaphthoxazine derivative (222) (0.39 g; 100%)

which formed yellow microcrystals, mp 149-150°C [from light petroleum (bp 80-100°C)], ν_{max} 2218 (C≡N) cm^{-1}, δ_H ($CDCl_3$) 8.32-8.28 (1H, m, ArH), 7.76-7.72 (1H, m, ArH), 7.54-7.38 (8H, m, ArH), 7.20-7.17 (4H, m, ArH) and 2.34 (6H, s, 2 x CH_3).

9,10-Phenanthrenedione 9-Oxime (226)

A suspension of 9,10-phenanthrenedione (225) (41.6 g; 0.2 mol) in ethanol (400 ml) was stirred and treated with hydroxylamine hydrochloride (15.3 g; 0.22 mol) added in one portion at room temperature. The suspension was then stirred and heated under reflux for 1 h.

The resulting orange suspension was rotary evaporated, the residue was treated with 10% w/v aqueous sodium hydrogen carbonate solution (100 ml), and the insoluble orange solid was collected then washed with ethanol to give 9,10-phenanthrenedione 9-oxime (226) as an orange-yellow solid (42.3 g; 95%), mp 160-162°C (lit,[153] 158°C).

9,10-Phenanthrenedione 9-Oxime Lithium Salt (227)

A solution of 9,10-phenanthrenedione 9-oxime (226) (22.3 g; 0.1 mol) in Analar acetone (900 ml) was stirred and treated in one portion at room temperature with a solution of lithium hydroxide monohydrate (4.2 g; 0.1 mol) in water (50.0 ml). The resulting green-brown solution was then stirred at room temperature for 0.5 h.

The resulting suspension of a green solid in a green-brown solution was filtered, the solid was slurried with dichloromethane and the resulting suspension briefly heated to reflux. The suspension was cooled to room temperature then filtered to give the lithium salt (227) as a brown solid (16.1 g; 70%), mp 288°C (decomp with gas evolution), ν_{max} 3600-3200 br (OH) and 1636 (C=O) cm^{-1}, which was used without further purification.

Rotary evaporation of the aqueous acetone mother liquor gave a brown solid (8.1 g) which was slurried with dichloromethane and the resulting suspension briefly heated to reflux. The cooled mixture was filtered to give a second, less pure crop of the lithium salt (227) as a brown solid (6.5 g; 28%), mp 258°C (decomp with gas evolution), identified by comparison (ir spectrum) with the sample obtained before.

9,10-Phenanthrenedione 9-Oxime Diarylformylmethyl Ethers (231)

(a) A suspension of 9,10-phenanthrenedione 9-oxime lithium salt (227) (2.5 g; 0.011 mol) in Analar acetone (80.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The brown suspension was stirred and treated dropwise at room temperature with a solution of the corresponding 2-bromo-2,2-diarylacetaldehyde (0.01 mol) in Analar acetone (20.0 ml) and the mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 1-15 h.

The resulting brown solution was rotary evaporated and the residue was treated with water (20.0 ml) then extracted several times with dichloromethane. Rotary evaporation of the combined dichloromethane extracts gave the crude product which was purified as described for the individual reactions below.

(i) The reaction of the lithium salt (227) with 2-bromo-2,2-diphenylacetaldehyde (228a) gave an orange-brown oil which was triturated with ether to afford 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a) (91%) which formed yellow microcrystals, mp 145-151°C (from 1,2-dimethoxyethane-ethanol), ν_{max} 1738 and 1682 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.05 (1H, s, CH=O), 8.80-8.75 (1H, m, ArH), 8.10-7.97 (3H, m, ArH) and 7.71-7.33 (14H, m, ArH).

(ii) The reaction of the lithium salt (227) with 2-bromo-2,2-(di-4-methylphenyl)acetaldehyde (228b) gave a brown gum which was triturated with ether to afford 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)-formylmethyl ether (231b) (45%) which formed yellow microcrystals, mp 156-158°C [from toluene-light petroleum (80-100°C)], ν_{max} 1732 and 1679 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.01 (1H, s, CH=O), 8.80-8.75 (1H, m, ArH), 8.11-7.96 (2H, m, ArH), 7.70-7.15 (13H, m, ArH) and 2.34 (6H, s, 2 x CH_3).

(iii) The reaction of the lithium salt (227) with 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (228c) gave a red-brown oil which was flash-chromatographed over silica.

Elution with hexane-ether (17:3) gave 9,10-phenanthrenedione 9-oxime (226) as an orange solid (37%), mp 132-135°C (lit, [153]158°C), identified by comparison (ir and ^{1}H nmr spectra) with an authentic sample.

Further elution with hexane-ether (17:3) gave 9,10-phenanthrenedione 9-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (231c) (40%) which formed yellow microcrystals, mp 165-167°C (decomp) [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1743 and 1682 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.05 (1H, s, CH=O), 8.69-8.65 (1H, m, ArH), 8.10-7.99 (3H, m, ArH) and 7.75-7.41 (12H, m, ArH).

Elution with ether gave 9,10-phenanthrenedione 9-oxime 2-oxopropyl ether (230) (30%) which formed orange microcrystals, mp 134-137°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1723 and 1670 (C=O) cm^{-1}, δ_H ($CDCl_3$) 8.63 (1H, dd, J 7.7 and 1.4 Hz, ArH), 8.10 (1H, dd, J 16.2 and 1.2 Hz, ArH), 8.01-7.03 (2H, m, ArH), 7.69-7.35 (4H, m, ArH), 5.02 (2H, s, CH_2) and 2.19 (3H, s, CH_3).

(iv) Reaction of the lithium salt (227) with 9-bromofluorene-9-carboxaldehyde (195) gave a 10:1 mixture of the *syn* and *anti* isomers of 9,10-phenanthrenedione 9-oxime 9-formylfluoren-9-yl ether (236) (82%) which formed yellow microcrystals, mp 165-168°C (from ethanol-dimethylformamide), ν_{max} 1733 and 1676 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.88 (1H, s, CH=O) (*anti*), 9.71 (1H, s, CH=O) (*syn*), 8.62-8.57 (2H, m, ArH) (*syn* and *anti*), 8.22-8.09 (2H, m,

ArH) (*syn* and *anti*), 8.01-7.92 (6H, m, ArH) (*syn* and *anti*), 7.85-7.62 (10H, m, ArH) (*syn* and *anti*) and 7.54-7.27 (12H, m, ArH) (*syn* and *anti*).

(b) A suspension of 9,10-phenanthrenedione 9-oxime lithium salt (227) (2.5 g; 0.011 mol) in anhydrous 1,2-dimethoxyethane (80.0 ml) was stirred and briefly heated under to then cooled to room temperature. The brown suspension was stirred and treated dropwise at room temperature with a solution of the corresponding 2-halogeno-2,2-diarylacetaldehyde (0.01 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 1-2 h.

The resulting brown solution was rotary evaporated and the residue treated with water (20.0 ml) then extracted several times with dichloromethane, with filtration to remove any unreacted lithium salt, and the combined dichloromethane extracts rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The reaction of the lithium salt (227) with 2-bromo-2,2-di-(4-trifluoromethylphenyl)acetaldehyde (228c) gave unreacted lithium salt (227) (3%), and from the dichloromethane extracts, a brown gum which was washed with ether to give a yellow solid. This was combined with a second crop obtained by rotary evaporation of the ether mother liquor and flash-chromatography of the residual brown gum over silica, eluting with hexane-ether (4:1) to give 9,10-phenanthrenedione 9-oxime di-(4-

trifluoromethylphenyl)formylmethyl ether (231c) as a yellow solid (total 63%), mp 165-167°C, identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(ii) The reaction of the lithium salt (227) with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (229e) gave unreacted lithium salt (227) (26%), and from the dichloromethane extracts, an orange-brown gum which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave 9,10-phenanthrenedione 9-oxime (226) as a yellow solid (7%), mp 130-137°C, identified by comparison (ir spectrum) with an authentic sample.

Elution with hexane-dichloromethane (1:9) gave an oily yellow solid which was washed with light petroleum (bp 40-60°C) to give a 4:1 mixture of the *syn* and *anti* isomers of 9,10-phenanthrenedione 9-oxime di-(4-methoxyphenyl)-formylmethyl ether (231e) (9%) which formed yellow microcrystals, mp 159-161°C (decomp) (from hexane-ethyl acetate), ν_{max} 1737 and 1658 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.96 (1H, s, CH=O) (*anti*), 9.91 (1H, s, CH=O) (*syn*), 8.75 (1H, dd, J 7.7 and 1.7 Hz, ArH) (*anti*), 8.23 (1H, dd, J 8.0 and 1.2 Hz, ArH) (*syn*), 8.11-7.21 (22H, m, ArH) (*syn* and *anti*), 6.95-6.85 (8H, m, ArH) (*syn* and *anti*) and 3.79 (12H, s, 4 x CH_3) (*syn* and *anti*).

Further elution with hexane-dichloromethane (1:9) gave an orange-yellow solid which was washed with ether to give the *anti* isomer of the oxime ether (231e) (38%) which formed yellow microcrystals, mp 137-139°C (from hexane-ethyl acetate), ν_{max} 2725 (CH=O) and 1739 and 1677 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.96 (1H, s, CH=O), 8.75 (1H, dd, J 7.7 and 1.7 Hz, ArH), 8.11-7.96 (3H, m, ArH), 7.71-7.33 (8H, m, ArH), 6.93-6.86 (4H, m, ArH) and 3.79 (6H, s, 2 x CH_3).

The Attempted Reaction of 9,10-Phenanthrenedione 9-Oxime Lithium Salt (227) with Bromoacetone

A suspension of 9,10-phenanthrenedione 9-oxime lithium salt (227) (1.1 g; 0.005 mol) in Analar acetone (40.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The brown suspension was stirred and treated dropwise at room temperature with a solution of bromoacetone (0.69 g; 0.005 mol) in Analar acetone (10.0 ml) and the resulting suspension was stirred at room temperature with the exclusion of atmospheric moisture for 20 h.

The resulting brown solution was rotary evaporated to give a gummy brown solid (1.7 g) which was treated with dichloromethane (5.0 ml) and the insoluble solid collected to give the impure lithium salt (227) as a brown solid (0.50 g; 45%), mp 238°C (decomp), identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

Rotary evaporation of the dichloromethane filtrate gave 9,10-phenanthrenedione 9-oxime (226) as a brown solid (0.60 g; 54%), mp 158-162°C (lit,[153] 160-161°C), identified by comparison (mp and ir spectrum) with an authentic sample.

The Attempted Reaction of 9,10-Phenanthrenedione 9-Oxime Lithium Salt (227) with 2-Bromo-2,2-di-(4-*N*,*N*-dimethylaminophenyl)acetaldehyde (228d)

(a) A suspension of 9,10-phenanthrenedione 9-oxime lithium salt (227) (1.3 g; 0.0055 mol) in Analar acetone (40.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The suspension was stirred and treated dropwise with a solution of 2-bromo-2,2-di-(4-*N*,*N*-dimethylamino-phenyl)acetaldehyde (228d) (1.8 g; 0.005 mol) in Analar acetone (10.0 ml) and the resulting brown suspension was stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The brown suspension was rotary evaporated and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane (5.0 ml), with initial filtration to give the unreacted lithium salt (227) as a brown solid (1.2 g; 92%), mp 227°C (decomp with gas evolution), identified by comparison [ir spectrum and tlc in hexane-ether (2:3) over silica] with a sample prepared before. Rotary evaporation of the combined dichloromethane extracts gave a brown gum (0.93 g) which yielded no identifiable material.

(b) Repetition of the reaction described in (a) before, but at reflux for 6 h gave unreacted lithium salt (227) (89%), and from the dichloromethane extracts, a brown gum which yielded no identifiable product.

2,2-Diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines

(a) A solution of the corresponding 9,10-phenanthrenedione 9-oxime diarylformylmethyl ether (0.004 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml) was stirred and treated at room temperature with a solution of triphenylphosphine (2.1 g; 0.008 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 15 h.

The resulting brown solution was rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(i) The gum obtained from the reaction of 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave a gummy yellow-orange solid. This was washed with light petroleum (bp 40-60°C) to give 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) (40%) which formed cream microcrystals, mp 183-185°C (from toluene-light petroleum), δ_H ($CDCl_3$) 8.65-8.44 (4H, m, ArH), 8.09 (1H, s, CH) and 7.71-7.23 (14H, m, ArH), δ_C ($CDCl_3$) 155.4 (CH), 144.1 (quat), 137.8 (quat), 131.0 (quat), 129.9 (quat), 129.5 (quat),

128.7 (quat), 128.6 (quat), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 124.9 (CH), 122.8 (quat), 122.6 (CH), 122.5 (CH), 122.3 (CH), 122.3 (CH) and 79.4 (quat), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

(ii) The brown gum obtained from the reaction of 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) (53%) which formed cream microcrystals, mp 151-152°C [from light petroleum (bp 80-100°C)], δ_H ($CDCl_3$) 8.64-8.43 (4H, m, ArH), 8.09 (1H, s, CH), 7.71-7.45 (4H, m, ArH), 7.42-7.21 (4H, m, ArH), 7.15-7.11 (4H, m, ArH) and 2.30 (6H, s, 2 x CH_3), δ_C ($CDCl_3$) 155.8 (CH), 138.2 (quat), 138.0 (quat), 137.9 (quat), 131.0 (quat), 130.0 (quat), 129.6 (quat), 129.1 (CH), 127.3 (CH), 127.1 (CH), 126.8 (CH), 126.7 (quat), 126.6 (CH), 125.1 (quat), 124.8 (CH), 122.8 (quat), 122.7 (CH), 122.6 (CH), 122.5 (CH), 122.3 (CH), 79.3 (quat) and 21.0 (CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a red-brown spot which faded on removal of the irradiation source.

(iii) The red-brown gum obtained from the reaction of 9,10-phenanthrenedione 9-oxime di-(4-trifluoromethylphenyl)formylmethyl ether (231c) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted triphenylphosphine as a colourless solid (1.4 g), mp 75-80°C (lit,[164] 80°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with an authentic sample.

Further elution with hexane-ether (9:1) gave a brown gum which was triturated with light petroleum (bp 40-60°C) and the insoluble solid was collected to give 2,2-di-(4-trifluoromethylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232c) (5%) which formed cream microcrystals, mp 198-201°C [from toluene-light petroleum (bp 80-100°C)], δ_H ($CDCl_3$) 8.65-8.42 (4H, m, ArH), 8.04 (1H, s, CH) and 7.71-7.55 (12H, m, ArH), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

Further elution with hexane-ether (9:1) through to ether gave only a series of intractable solids from which no identifiable material could be obtained.

(iv) The red gum from the reaction of 9,10-phenanthrenedione 9-oxime di-(4-methoxyphenyl)formylmethyl ether (231e) was flash-chromatographed over silica.

Elution with hexane-ether (4:1) afforded 2,2-di-(4-methoxyphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232e) (70%) which formed beige microcrystals, mp 151-153°C (from acetonitrile), ν_{max} 1634 (C=N) cm^{-1}, δ_H ($CDCl_3$) 8.63-8.42 (4H, m, ArH), 8.02 (1H, s, CH), 7.70-7.50 (4H, m, ArH), 7.44-7.36 (4H, m, ArH), 6.88-6.80 (4H, m, ArH) and 3.74 (6H, s, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a purple-red spot which faded on removal of the irradiation source.

(b) A solution of 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a) (0.83 g; 0.002 mol) in anhydrous tetrahydrofuran (10.0 ml) was stirred and treated in one portion at room temperature with triphenylphosphine (1.0 g; 0.004 mol) in anhydrous tetrahydrofuran (10.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 29 h.

The resulting red-brown solution was allowed to cool then rotary evaporated to give a red-brown gum (2.0 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) gave a gummy cream solid (0.17 g) which was washed with light petroleum to give the phenanthro-oxazine derivative (232a) as a cream solid (0.09 g; 11%), mp 134-136°C, identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with a previously prepared sample.

Further elution with hexane-dichloromethane (7:3) gave unreacted 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a) as a yellow solid (0.15 g; 18%), mp 144°C (decomp), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

Further elution with hexane-dichloromethane (7:3) to dichloromethane gave only a series of intractable oils and solids (total 0.69 g) from which no identifiable product was isolated.

(c) A solution of 9,10-phenanthrenedione 9-oxime diphenylformylmethyl ether (231a) (0.83 g; 0.002 mol) in anhydrous 1,4-dioxane (10.0 ml) was stirred and treated at room temperature in one portion with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,4-dioxane (10.0 ml). The resulting solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 6 h.

The brown solution was rotary evaporated to give a brown gum (1.9 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) gave a gummy orange solid (0.38 g) which was washed with light petroleum to give the phenanthro-oxazine derivative (232a) as a beige solid (0.27 g; 35%), mp 171-173°C, identified by

comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with a previously prepared sample.

3,4-Dihydro-2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (233)

A solution of the corresponding 2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233) (0.0003 mol) in 1,2-dimethoxyethane (3.0 ml) was stirred and treated dropwise at room temperature over 15 min with a solution of sodium borohydride (0.06 g; 0.0015 mol) in water (0.75 ml) and the resulting solution was stirred at room temperature for 5 h.

The resulting pale yellow suspension was rotary evaporated and the residue was treated with water (1.5 ml) then extracted several times with dichloromethane to give the crude product which was purified as described for the individual reactions below.

(a) The reaction with 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) gave 3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233a) (100%) which formed cream microcrystals, mp 233-235°C (from toluene), ν_{max} 3406 (NH) and 1622 (NH def) cm^{-1}, δ_H ($CDCl_3$) 8.67-8.57 (2H, m, ArH), 7.70-7.19 (16H, m, ArH), 4.00-3.00 (2H, brs, CH_2) and 2.10-1.60 (1H, brs, NH) (exch), on D_2O shake becomes 8.61-8.51 (2H, m, ArH), 7.81-7.19 (16H, m, ArH) and 4.03 (2H, brs, CH_2).

(b) The reaction with 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) gave 3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233b) (77%) which formed pale yellow microcrystals, mp 244-246°C (from ethanol-dimethylformamide), ν_{max} 3400 (NH) and 1621 (NH def) cm^{-1}, δ_H [$(CD_3)_2SO$] 8.71-8.64 (2H, m, ArH), 8.37 (1H, d, J 7.3 Hz, ArH), 7.99-7.94 (1H, m, ArH), 7.72-7.44 (8H, m, ArH), 7.08 (4H, d, J 8.1 Hz, ArH), 6.04 (1H, s, NH) (exch), 4.04 (2H, d, J 4.5 Hz, CH_2) and 3.37 (6H, s, 2 x CH_3).

The Oxidation of 3,4-Dihydro-2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (233) with Manganese Dioxide to give 2,2-Diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (232)

A solution of the corresponding 3,4-dihydro-2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233) (0.00025 mol) in 1,2-dimethoxyethane (5.0 ml) was stirred and treated at room temperature with activated manganese dioxide (0.13 g) added in one portion. The resulting suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The suspension was filtered through celite and the filtrate rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(a) The reaction with 3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233a) gave 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) as a yellow solid (100%), mp 184-185°C, identified by comparison [mp, ir

spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(b) The reaction with 3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233b) gave 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) as a yellow solid (90%), mp 150-153°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (7:3) over silica] with a sample prepared before.

3-Cyano-3,4-dihydro-2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (234)

A solution of the corresponding 2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232) (0.001 mol) in glacial acetic acid (10.0 ml) was stirred and treated at room temperature with potassium cyanide (0.33 g; 0.005 mol) added in one portion. The resulting mixture was then stirred and heated at 100°C for 6 h. The resulting brown solution was cooled then allowed to stand at room temperature for 15 h.

The suspension was rotary evaporated under high vacuum (oil pump) and the residue was treated with water (5.0 ml) then extracted several times with dichloromethane. The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(a) The reaction with 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) gave a yellow foam which was triturated with light petroleum (bp 40-60°C) to afford 3-cyano-3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (234a) (73%) which formed colourless microcrystals, mp 238-240°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 3391 (NH) and 1630 (NH def) cm^{-1}, δ_H ($CDCl_3$) 8.65-8.58 (4H, m, ArH), 7.81-7.09 (14H, m, ArH), 5.46 (1H, s, CH) and 4.57 (1H, s, NH) (exch).

(b) The reaction with 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) gave a yellow foam which was triturated with ether-light petroleum (bp 40-60°C) to afford 3-cyano-3,4-dihydro-2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (234b) (55%) which formed cream microcrystals, mp 238-241°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 3366 (NH), 2241 w (C≡N) and 1631 (NH def) cm^{-1}, δ_H ($CDCl_3$) 8.63-8.53 (4H, m, ArH), 7.75-7.14 (10H, m, ArH), 7.01-6.98 (2H, m, ArH), 5.40 (1H, s, CH), 4.80-3.90 (1H, brs, NH) (exch), 2.34 (3H, s, CH_3) and 2.17 (3H, s, CH_3).

3-Cyano-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (235a)

A solution of 3-cyano-3,4-dihydro-2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (234a) (0.41 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was stirred and treated at room temperature with activated manganese dioxide (0.50 g) added in one portion. The resulting solution was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The suspension was filtered through celite and the filtrate rotary evaporated to give the cyanophenanthro-oxazine derivative (235a) (0.41 g; 100%) which formed yellow microcrystals, mp 219-220°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 2219 (C≡N) and 1611 (C=N) cm^{-1}, δ_H ($CDCl_3$) 8.60-8.43 (4H, m, ArH), 7.76-7.56 (8H, m, ArH) and 7.55-7.35 (6H, m, ArH).

The Reaction of a Mixture of 9,10-Phenanthrenedione 9-Oxime Di-(4-methylphenyl)formylmethyl Ether (231b) and *Anti*-1,2-naphthalenedione 2-Oxime Diphenylformylmethyl Ether (122) with Triphenylphosphine in 1,2-Dimethoxyethane

A solution of 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b) (1.6 g; 0.0035 mol) in anhydrous 1,2-dimethoxyethane (26.0 ml) was mixed with a solution of *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) (1.3 g; 0.035 mol) in anhydrous 1,2-dimethoxyethane (17.0 ml) and the mixture was stirred and treated with a solution of triphenylphosphine (3.7 g; 0.014 mol) in anhydrous 1,2-dimethoxyethane (18.0 ml) added in one portion. The resulting solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 15 h.

The resulting brown solution was allowed to cool then was rotary evaporated and the residual brown gum (6.9 g) was flash-chromatographed over silica.

Elution with hexane-dichloromethane (11:9) gave a brown oil (0.78 g) which was triturated with ether-light petroleum (bp 40-60°C) to give a grey solid (0.47 g) shown by mass spectroscopy to be an unresolvable mixture of 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) [Found: m/z (HREIMS) 385.1463 (M^+), $C_{28}H_{19}NO$ requires: M, 385.1467] and 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232b) [Found: m/z (HREIMS) 413.1796 (M^+), $C_{30}H_{23}NO$ requires: M, 413.1780].

Elution with hexane-dichloromethane (7:13) gave a brown oil (0.60 g) which was triturated with ether-light petroleum (bp 40-60°C) to give a beige solid (0.32 g) shown by mass spectroscopy to be an unresolvable mixture of 2,2-diphenyl-2*H*-naphth[1,2-*b*]-1,4-oxazine (123) [Found: m/z (HREIMS) 335.1311 (M^+), $C_{24}H_{17}NO$ requires: M, 335.1310] and 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) [Found: m/z (HREIMS) 363.1632 (M^+), $C_{26}H_{21}NO$ requires: M, 363.1623].

The Thermolysis of a Mixture of *Anti*-1,2-naphthalenedione 2-Oxime Diphenylformylmethyl Ether (122) and 9,10-Phenanthrenedione 9-Oxime Di-(4-methylphenyl)formylmethyl Ether (231b)

A solution of 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b) (0.89 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was stirred and treated in one portion at room temperature with a solution of *anti*-1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) (0.73 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml). The resulting

solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 16 h.

The resulting brown solution was rotary evaporated to give a brown gum (1.7 g) which was shown by comparison [tlc in hexane-ether (1:1) over silica] to be a mixture of the starting materials (122) and (231b). The mixture of 1,2-naphthalenedione 2-oxime diphenylformylmethyl ether (122) and 9,10-phenanthrenedione 9-oxime di-(4-methylphenyl)formylmethyl ether (231b) (1.7 g) was dissolved in anhydrous 1,2-dimethoxyethane (40.0 ml) and the solution was heated under reflux with the exclusion of atmospheric moisture for 16 h.

The resulting brown solution was rotary evaporated to give an intractable brown gum (1.7 g) the mass spectrum of which, m/z (FABMS) 414, showed the absence of both starting materials (122) and (231b) or any possible oxime ether product.

The Attempted Reaction of 9,10-Phenanthrenedione 9-Oxime 9-Formylfluoren-9-yl Ether (236) with Triphenylphosphine in 1,2-Dimethoxyethane

A suspension of 9,10-phenanthrenedione 9-oxime 9-formylfluoren-9-yl ether (236) (0.83 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (30.0 ml) was stirred and treated in one portion at room temperature with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0

ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 15 h.

The resulting red-brown solution was cooled to room temperature then rotary evaporated to give a red-brown oil (1.9 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:1) through dichloromethane to methanol gave only a series of multi-component gums (total 1.6 g) from which no identifiable material could be obtained.

9,10-Phenanthrenedione 9-Imine (238)

A suspension of 9,10-phenanthrenedione (225) (4.2 g; 0.02 mol) in dichloromethane (100 ml) and ethanol (150 ml) was stirred and heated under reflux. The resulting orange solution was then treated with a slow stream of ammonia gas for 10 min at reflux to achieve saturation and then for a further 35 min.

The solution was concentrated to one third of its original volume by distillation of the solvent at atmospheric pressure under an atmosphere of ammonia. The resulting yellow-brown suspension was cooled to room temperature then filtered to give the phenanthrenedione imine (238) as a yellow solid (3.8 g; 92%), mp 157-159°C (lit,[154] 156-157°C), m/z (EIMS) 207 (M^+), ν_{max} 3200 (NH) and 1675 (C=O) cm^{-1}, δ_H ($CDCl_3$) 177.6 (quat), 161.9 (quat), 137.1 (quat),

135.6 (CH), 132.4 (CH), 132.0 (quat), 130.7 (quat), 129.8 (CH), 129.2 (quat), 129.1 (CH), 128.5 (quat), 127.4 (CH), 123.5 (CH) and 123.3 (CH).

Reactions of 9,10-Phenanthrenedione 9-Imine (238) with 1,1-Diarylethenes (239) to give 3,4-Dihydro-2,2-diaryl-2*H*-phenanthro[9,10-*b*]-1,4-oxazines (233)

(a) A solution of 9,10-phenanthrenedione 9-imine (238) (0.41 g; 0.002 mol) in anhydrous 1,4-dioxane (5.0 ml) was stirred and treated in one portion at room temperature with a solution of 1,1-diphenylethene (239a) (0.36 g; 0.002 mol) in anhydrous 1,4-dioxane (5.0 ml) and the stirred solution was heated under reflux with the exclusion of atmospheric moisture for 22 h.

The resulting brown solution was rotary evaporated to give a brown gum (0.76 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted 1,1-diphenylethene (239a) as a yellow oil (0.34 g; 94%) identified by comparison [ir spectrum and tlc in hexane-dichloromethane (3:2) over silica] with an authentic sample.

Elution with hexane-ether (9:1) gave a gum (0.11 g) whose tlc in hexane-dichloromethane (2:3) over silica showed the presence of 2,2-diphenyl-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (232a) and its 3,4-dihydro derivative (233a), identified by comparison with samples prepared before.

Elution with hexane-ether (7:3) through ether and ethyl acetate to methanol gave only a series of intractable gums and solids (total 0.24 g) from which no identifiable product was isolated.

(b) A solution of 9,10-phenanthrenedione 9-imine (238) (0.41 g; 0.002 mol) in anhydrous 1,4-dioxane (5.0 ml) was stirred and treated in one portion with a solution of 1,1-di-(4-*N,N*-dimethylaminophenyl)ethene (239d) (0.53 g; 0.002 mol) in anhydrous 1,4-dioxane (5.0 ml) and the resulting solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 2 h.

The resulting dark green solution was allowed to cool then was rotary evaporated to give a dark green solid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) to hexane-ethyl acetate (3:2) gave only a series of intractable gums and solids (total 0.81 g) from which no identifiable product was isolated.

Elution with ethyl acetate gave 3,4-dihydro-2,2-di-(4-*N,N*-dimethylaminophenyl)-2*H*-phenanthro[9,10-*b*]-1,4-oxazine (233d) as a yellow solid (0.09 g; 10%), mp 208-210°C.

5,6-Quinolinedione 5-Oxime (241)

A solution of 6-hydroxyquinoline (240) (21.8 g; 0.15 mol) in glacial acetic acid (190 ml) was stirred and cooled to 10°C (ice-water bath) then treated dropwise over 30 min with a solution of sodium nitrite (10.4 g; 0.15 mol) in water (75.0 ml). The resulting solution was stirred at 10°C for 1 h then at room temperature for 2 h.

The resulting green-brown suspension was concentrated by rotary evaporation under high vacuum (oil pump) to one third of its original volume, then diluted with water (115 ml). The resulting suspension was filtered to give 5,6-quinolinedione 5-oxime (241) as a green solid (22.7 g; 87%), mp 178°C (decomp with gas evolution) [lit,[155] 180°C (decomp)], ν_{max} 3050-2500 br (OH) and 1654 (C=N) cm^{-1}.

5,6-Quinolinedione 5-Oxime Lithium Salt (242)

A solution of 5,6-quinolinedione 5-oxime (241) (20.9 g; 0.12 mol) and lithium hydroxide monohydrate (5.0 g; 0.12 mol) in water (120 ml) was treated with Analar acetone (300 ml) and the resulting green suspension was stirred at room temperature for 30 min.

The green suspension was filtered and the solid washed with acetone to give the lithium salt (242) as a green solid (16.2 g; 68%), mp 214°C (decomp), ν_{max} 3600-2600 br (OH) and 1623 (C=O) cm^{-1}, which was used without further purification.

5,6-Quinolinedione 5-Oxime Diarylformylmethyl Ethers (243)

A suspension of 5,6-quinolinedione 5-oxime lithium salt (242) (1.0 g; 0.0055 mol) in anhydrous 1,2-dimethoxyethane (40.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The resulting green suspension was stirred and treated dropwise at room temperature with a solution of the corresponding 2-halogeno-2,2-diarylacetaldehyde (0.005 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 19-88 h.

The resulting mixture was filtered to remove any unreacted lithium salt (242), the filtrate was rotary evaporated and the residue was treated with water (10.0 ml) then extracted several times with dichloromethane to give the crude product which was purified as described for the individual reactions below.

(a) The reaction of the lithium salt (242) with 2-bromo-2,2-diphenylacetaldehyde (203a) gave a gummy yellow-brown solid which was washed with ether to afford the 5,6-quinolinedione 5-oxime diphenylformylmethyl ether (243a) (78%) which formed yellow microcrystals, mp 143-145°C (from ethyl acetate-light petroleum), ν_{max} 1725 and 1678 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.03 (1H, s, CH=O), 9.16 (1H, ddd, J 9.2, 1.6 and 0.6 Hz, H_4), 8.68 (1H, dd, J 4.8 and 1.6 Hz, H_2), 7.58 (1H, dd, J 10.2 and 0.6 Hz, H_8), 7.56-7.36 (11H, m, ArH and H_3) and 6.57 (1H, d, J 10.2 Hz, H_7).

(b) The reaction of the lithium salt (242) with 2-bromo-2,2-di-(4-methylphenyl)acetaldehyde (203b) gave unreacted lithium salt (40%), and from the dichloromethane extracts, a brown gum which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (4:1) gave the *syn* isomer of 5,6-quinolinedione 5-oxime di-(4-methylphenyl)formylmethyl ether (243b) (4%) which formed orange microcrystals, mp 167°C (decomp) [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1726 and 1651 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.91 (1H, s, CH=O), 8.64 (1H, dd, J 4.7 and 1.7 Hz, H_2), 8.10 (1H, ddd, J 9.0, 1.6 and 0.6 Hz, H_4), 7.59 (1H, dd, J 10.2 and 0.6 Hz, H_8), 7.43 (4H, d, J 8.1 Hz, ArH), 7.28 (1H, dd, J 9.0 and 4.7 Hz, H_3), 7.19 (4H, d, J 8.1 Hz, ArH), 6.60 (1H, d, J 10.2 Hz, H_7) and 2.34 (6H, s, 2 x CH_3).

Further elution with hexane-ethyl acetate (4:1) gave the *anti* isomer of 5,6-quinolinedione 5-oxime di-(4-methylphenyl)formylmethyl ether (30%) which formed yellow needles, mp 132-134°C (from ethanol), ν_{max} 1731 and 1671 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.99 (1H, s, CH=O), 9.17 (1H, ddd, J 9.0, 1.6 and 0.5 Hz, H_4), 8.65 (1H, dd, J 4.8 and 1.6 Hz, H_2), 7.56 (1H, dd, J 10.2 and 0.6 Hz, H_8), 7.36 (1H, dd, J 9.0 and 4.8 Hz, H_3), 7.30 (4H, d, J 8.1 Hz, ArH), 7.19 (4H, d, J 8.1 Hz, ArH), 6.54 (1H, d, J 10.2 Hz, H_7) and 2.35 (6H, s, 2 x CH_3).

(c) The reaction of the lithium salt (242) with 2-chloro-2,2-di-(4-methoxyphenyl)acetaldehyde (204c) gave unreacted lithium salt (242) (38%),

and from the dichloromethane extracts, a brown gum which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (4:1) gave a 5:2 mixture of the *syn* and *anti* isomers of 5,6-quinolinedione 5-oxime di-(4-methoxyphenyl)formylmethyl ether (243c) (37%) which formed orange microcrystals, mp 156-158°C (decomp) (from ethyl acetate), ν_{max} 1720 and 1651 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.94 (1H, s, CH=O) (*anti*), 9.86 (1H, s, CH=O) (*syn*), 9.15 (1H, ddd, J 8.2, 1.6 and 0.6 Hz, H_4) (*anti*), 8.69-8.63 (2H, m, H_2) (*syn* and *anti*), 8.12 (1H, ddd, J 8.2, 1.6 and 0.6 Hz, H_4) (*syn*), 7.64-7.25 (12H, m, ArH and H_3 and H_7) (*syn* and *anti*), 6.95-6.87 (8H, m, ArH) (*syn* and *anti*), 6.60 (1H, d, J 10.2 Hz, H_7) (*syn*), 6.56 (1H, d, J 10.2 Hz, H_7) (*anti*) and 3.80 (12H, s, 4 x CH_3) (*syn* and *anti*).

3,3-Diaryl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazines (244)

A solution of the corresponding 5,6-quinolinedione 5-oxime diarylformylmethyl ether (243) (0.001 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was stirred and treated in one portion at room temperature with a solution of triphenylphosphine (0.52 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 20 h.

The resulting brown solution was rotary evaporated to give the crude product which was purified as described for the individual reactions below.

(a) The brown gum obtained from the reaction of 5,6-quinolinedione 5-oxime diphenylformylmethyl ether (243a) was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (13:7) gave 3,3-diphenyl-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine (244a) (25%) which formed colourless microcrystals, mp 207-209°C (from ethyl acetate-light petroleum), δ_H ($CDCl_3$) 8.82-8.78 (2H, m, ArH), 8.03 (1H, s, CH), 7.95 (1H, d, J 9.2 Hz, ArH) and 7.46-7.27 (12H, m, ArH), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

(b) The brown gum obtained from the reaction of the *anti* isomer of 5,6-quinolinedione 5-oxime di-(4-methylphenyl)formylmethyl ether (243b) was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (7:3) gave 3,3-di-(4-methylphenyl)-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine (244b) (41%) which formed colourless microcrystals, mp 194-196°C (from toluene), δ_H ($CDCl_3$) 8.80-8.75 (2H, m, ArH), 8.00 (1H, s, CH), 7.92 (1H, d, J 9.2 Hz, ArH), 7.44-7.25 (6H, m, ArH), 7.18-7.13 (4H, m, ArH) and 2.31 (6H, m, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a red spot which faded on removal of the irradiation source.

(c) The brown gum obtained from the reaction of a 5:2 mixture of the *syn* and *anti* isomers of 5,6-quinolinedione 5-oxime di-(4-methoxyphenyl)formyl-methyl ether (243c) was flash-chromatographed over silica.

Elution with hexane-ether (1:1) gave 3,3-di-(4-methoxyphenyl)-3*H*-pyrido[3,2-*f*]-1,4-benzoxazine (244c) (76%) which formed cream microcrystals, mp 159-160°C [from toluene-light petroleum (bp 80-100°C)], δ_H ($CDCl_3$) 8.81-8.76 (2H, m, ArH), 7.94 (1H, s, CH), 7.92 (1H, d, J 9.1 Hz, ArH), 7.43-7.18 (6H, m, ArH), 6.90-6.84 (4H, m, ArH) and 3.76 (6H, m, 2 x CH_3), which was photochromic on a silica tlc plate, irradiation at 254 nm giving a brown spot which faded on removal of the irradiation source.

1,2-Acenaphthylenedione 1-Oxime (246)

A suspension of 1,2-acenaphthylenedione (245) (18.2 g; 0.1 mol) in ethanol (200 ml) was stirred and treated with hydroxylamine hydrochloride (7.6 g; 0.11 mol) added in one portion, and the suspension was stirred and heated under reflux for 1 h.

The resulting suspension of a beige solid in an orange-brown solution was cooled to room temperature then rotary evaporated. The residue was treated with water (200 ml) and the insoluble solid collected to give 1,2-acenaphthylenedione 1-oxime (246) as a beige solid (19.7 g; 100%), mp 205°C (decomp) (lit,[156] 207°C/230°C), ν_{max} 3500-3100 br (OH), 1731 (C=O) and 1647 (C=N) cm^{-1}.

1,2-Acenaphthylenedione 1-Oxime Lithium Salt (247)

A solution of 1,2-acenaphthylenedione 1-oxime (246) (2.0 g; 0.01 mol) in Analar acetone (90.0 ml) was stirred and treated in one portion at room temperature with a solution of lithium hydroxide monohydrate (0.42 g; 0.01 mol) in water (5.0 ml) and the resulting orange solution was stirred at room temperature for 30 min.

The resulting suspension of a yellow solid in an orange solution was filtered to give the lithium salt (247) as a yellow solid (1.8 g; 88%), mp 262°C (decomp), ν_{max} 3600-2700 br (OH) and 1690 (C=O) cm^{-1}, which was used without further purification.

1,2-Acenaphthylenedione 1-Oxime Diphenylformylmethyl Ether (248)

A suspension of 1,2-acenaphthylenedione 1-oxime lithium salt (247) (1.1 g; 0.0055 mol) in anhydrous 1,2-dimethoxyethane (40.0 ml) was stirred and briefly heated to reflux then cooled to room temperature. The suspension was then treated dropwise at room temperature with a solution of 2-bromo-2,2-diphenylacetaldehyde (203a) (1.4 g; 0.005 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the suspension stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The resulting yellow-orange solution was rotary evaporated, the residue was treated with water (10.0 ml) and the insoluble solid collected to give the oxime ether (248) (1.6 g; 82%) which formed cream microcrystals, mp 204-206°C

(decomp) (from toluene), ν_{max} 2729 (CH=O) and 1734 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.18 (1H, s, CH=O), 8.50-8.46 (1H, m, ArH), 8.11-6.98 (4H, m, ArH), 7.76-7.67 (2H, m, ArH) and 7.60-7.33 (9H, m, ArH).

Attempted Reactions of 1,2-Acenaphthylenedione 1-Oxime Diphenylformylmethyl Ether (248) with Triphenylphosphine

(a) A solution of 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248) (0.78 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated in one portion at room temperature with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 46 h.

The red-brown solution was allowed to cool then was rotary evaporated. The residual red-brown gum (2.0 g) was triturated with methanol and the insoluble solid was collected and combined with a second crop obtained by rotary evaporation of the methanol mother liquor and flash-chromatography of the residual gum (1.4 g) over silica eluting with hexane-ether (3:2) to give unreacted 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248) as a beige solid (total 0.60 g; 77%), mp 186-190°C, identified by comparison [ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

(b) A solution of 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248) (0.78 g; 0.002 mol) in anhydrous 1,4-dioxane (15.0 ml) was stirred and treated in one portion at room temperature with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,4-dioxane (10.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 63 h.

The resulting red-brown solution was cooled then rotary evaporated to give a gummy brown solid which was successively washed with methanol and ether to give the unreacted oxime ether (248) as a beige solid (0.60 g; 77%), mp 193°C (decomp), identified by comparison [mp, ir spectrum and tlc in hexane-ether (1:1) over silica] with a sample prepared before.

The Attempted Reaction of a Mixture of 1,2-Naphthalenedione 2-Oxime Di-(4-methylphenyl)formylmethyl Ether (216a) and 1,2-Acenaphthylenedione 1-Oxime Diphenylformylmethyl Ether (248) with Triphenylphosphine

A solution of 1,2-naphthalenedione 2-oxime di-(4-methylphenyl)formylmethyl ether (216a) (0.40 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was stirred and treated in one portion at room temperature with a solution of 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248) (0.39 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) followed by a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane

(5.0 ml) also added in one portion. The resulting solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 20 h.

The brown solution was rotary evaporated to give a brown gum (1.9 g) whose mass spectrum showed a peak, m/z (EIMS) 363 (M^+), due to 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a), but no evidence for the formation of the diphenylnaphthoxazine derivative (123). The crude gum (1.9 g) was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted triphenylphosphine as a grey solid (0.27 g), mp 79-81°C (lit,[164] 80°C), identified by comparison [mp and tlc in hexane-dichloromethane (2:3) over silica] with an authentic sample.

Further elution with hexane-ether (9:1) gave a gummy purple solid (0.19 g) which was washed with ether-light petroleum (bp 40-60°C) to give 2,2-di-(4-methylphenyl)-2*H*-naphth[1,2-*b*]-1,4-oxazine (218a) as a pale pink solid (0.10 g; 28%), mp 170-174°C, identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (3:7) over silica] with a sample prepared before.

Further elution with hexane-ether (9:1) gave a purple gum (0.15 g) which was triturated with ether and the insoluble purple solid collected to give unreacted 1,2-acenaphthylenedione 1-oxime diphenylformylmethyl ether (248) as a purple solid (0.10 g; 26%), mp 197-200°C (decomp), identified by comparison

[mp, ir spectrum and tlc in hexane-dichloromethane (3:7) over silica] with a sample prepared before.

Table 8: Elemental Analysis and Mass Spectroscopic Data

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(206) ($C_{12}H_{12}O_2$)	76.5	6.4	--	188	76.6	6.4	--	188
(205) ($C_{11}H_{10}O_2$)	75.9	5.8	--	174	75.9	5.7	--	174
(131a) ($C_{18}H_{22}O_2$)				(253.1585) [$(M+H)^+$-H_2O]				(253.1585) [$(M+H)^+$-H_2O]
(131b) ($C_{18}H_{16}F_6O_2$)	57.0	4.2	--	(361) [$(M+H)^+$-H_2O]	57.1	4.2	--	(379)
(131c) ($C_{20}H_{28}N_2O_2$)	73.2	8.5	8.5	310 [M^+-H_2O]	73.2	8.5	8.5	328
(175) ($C_{20}H_{26}O_2$)	80.8	9.0	--	(281) [$(M+H)^+$-H_2O]	80.5	8.7	--	(299)
(182) ($C_{24}H_{22}O_2$)	84.0	6.7	--	(325) [$(M+H)^+$-H_2O]	84.2	6.4	--	(343)
(130d) ($C_{18}H_{20}O_3$)	75.7	6.8	--	(285)	76.1	7.0	--	(285)
(133a) ($C_{16}H_{16}O$)				(225.1277)				(225.1279)
(133b) ($C_{16}H_{10}F_6O$)				(333.0712)				(333.0712)
(177) ($C_{18}H_{20}O$)				252.1538				252.1514
(133c) ($C_{18}H_{22}N_2O$) [b]				253 [M^+-CH=O]				282
(184) ($C_{22}H_{16}O$)	88.7	5.6	--	296	89.2	5.4	--	296
(133d) ($C_{16}H_{16}O_3$)				256.1098				256.1099
(193) ($C_{14}H_{10}O$)				194.0733				194.0732
(134a) ($C_{16}H_{15}BrO$)				223.1120 [M^+-Br]				223.1123 [M^+-Br]
(134b) ($C_{16}H_9BrF_6O$)				331.0563 [M^+-Br]				331.0558 [M^+-Br]
(134c)($C_{18}H_{21}{}^{79}BrN_2O$)				360.0836				360.0837
($C_{18}H_{21}{}^{81}BrN_2O$)				362.0697				362.0880

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy. [b] Product decomposed before high resolution mass spectrum could be aquired.

Table 8: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(187) ($C_{22}H_{14}Br_2O$)	58.4	3.0	--	(453, 455, 457)	58.2	3.1	--	(453, 455, 457)
(195) ($C_{14}H_9BrO$)	61.6	3.2	--	272, 274	61.5	3.3	--	272, 274
(152) ($C_{18}H_{22}O_3$)	75.4	7.7	--	no data	75.5	7.7	--	286
(163) ($C_{20}H_{26}O_5$)	69.6	7.5	--	346	69.4	7.5	--	346
(188) ($C_{26}H_{26}O_3$)	80.1	6.8	--	283 [M^+-$CH(OEt)_2$]	80.8	6.7	--	386
(164) ($C_{18}H_{20}O_4$)				300.1375				300.1372
(167) ($C_{16}H_{16}O_4$)	70.5	6.0	--	227 [M^+-CO_2H]	70.6	5.9	--	272
(144) ($C_{14}H_{12}O_2$)	78.9	5.9	--	212	79.3	5.7	--	212
(191) ($C_{22}H_{16}O_2$)	84.7	5.4	--	312	84.6	5.1	--	312
(190) ($C_{22}H_{16}O_2$)	84.1	5.2	--	312	84.6	5.1	--	312
(158) ($C_{14}H_{13}NO_2$)	74.2	5.7	6.2	227	74.0	5.7	6.2	227
(168) ($C_{16}H_{16}O_4$)	70.4	6.0	--	272	70.6	5.9	--	272
(169) ($C_{16}H_{16}O_4$)	70.5	5.9	--	272	70.6	5.9	--	272
(170) ($C_{16}H_{15}{}^{35}ClO_3$)				(291.0978)				(291.0788)
($C_{16}H_{15}{}^{37}ClO_3$)				(293.0759)				(293.0754)
(189) ($C_{22}H_{14}O_2$)				310.1005				310.0994
(135a) ($C_{26}H_{21}NO_3$) [b]	79.3	5.6	3.4	366 [M^+-CH=O]	79.0	5.3	3.5	395
(135a) ($C_{26}H_{21}NO_3$) [c]	79.5	5.3	3.7	366 [M^+-CH=O]	79.0	5.3	3.5	395

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy. [b] Mixture of *syn* and *anti* isomers. [c] *Anti* isomer.

Table 8: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(196) ($C_{24}H_{15}NO_3$)[d]	79.1	4.2	3.8	365	78.9	4.1	3.8	365
(196) ($C_{24}H_{15}NO_3$)[d]	79.1	4.0	3.9	336 [M^+-CH=O]	78.9	4.1	3.8	365
(171) ($C_{26}H_{21}NO_5$)[b]	72.9	5.2	3.2	398 [M^+-CH=O]	73.1	4.9	3.3	427
($C_{26}H_{21}NO_5$)[c]	73.3	5.2	3.3	398 [M^+-CH=O]	73.1	4.9	3.3	427
(201a) ($C_{25}H_{19}NO_4$)[b]	75.3	4.8	3.7	(398)	75.6	4.8	3.5	(398)
(201b) ($C_{27}H_{23}NO_4$)	76.4	5.9	3.3	(426)	76.2	5.4	3.3	(426)
(201c) ($C_{27}H_{23}NO_6$)	70.6	5.0	3.1	428 [M^+-CH=O]	70.9	5.0	3.1	457
(136) ($C_{13}H_{11}NO_3$)	68.5	4.8	6.0	229	68.1	4.8	6.1	229
(197) ($C_{24}H_{15}NO$)	86.1	4.5	4.1	333	86.5	4.5	4.2	333
(137a) ($C_{26}H_{21}NO$)	86.0	5.9	3.6	363	86.0	5.8	3.9	363
(172) ($C_{26}H_{21}NO_3$)	79.0	5.4	3.7	395	79.0	5.3	3.5	395
(202a) ($C_{25}H_{19}NO_2$)	81.9	5.3	3.7	(366)	82.2	5.2	3.8	(366)
(202b) ($C_{27}H_{23}NO_2$)	82.7	6.0	3.6	393	82.4	5.9	3.6	393
(202c) ($C_{27}H_{23}NO_4$)	76.0	5.5	3.1	425	76.2	5.4	3.3	425
(139) ($C_{26}H_{23}NO$)	85.3	6.4	3.6	(366)	85.5	6.3	3.8	(366)
(140) ($C_{27}H_{22}N_2O$)	83.2	5.8	6.8	(391)	83.1	5.6	7.2	(391)
(141) ($C_{27}H_{21}N_2O$)				(389.1663)				(389.1654)
(216a) ($C_{26}H_{21}NO_3$)	79.3	5.4	3.4	(396)	79.0	5.3	3.5	(396)

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy. [b] Mixture of *syn* and *anti* isomers. [c] *Anti* isomer. [d] Single isomer, geometry undefined.

Table 8: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(216b) ($C_{26}H_{15}F_6NO_3$)	62.0	2.9	2.8	(504)	62.0	3.0	2.8	(504)
(223) ($C_{24}H_{15}NO_3$)	78.9	4.1	3.6	365	78.9	4.1	3.8	365
(216d) ($C_{26}H_{21}NO_5$)	72.9	4.9	3.3	427	73.1	4.9	3.3	427
(218a) ($C_{26}H_{21}NO$)	85.7	5.8	3.6	363	86.0	5.8	3.9	363
(218b) ($C_{26}H_{15}F_6NO$)				471.1059				471.1057
(218d) ($C_{26}H_{21}NO_3$)	79.0	5.4	3.8	395	79.0	5.3	3.5	395
(224) ($C_{24}H_{15}NO$)				333.1154				333.1154
(220) ($C_{26}H_{23}NO$)	85.3	6.3	3.5	365	85.5	6.3	3.8	365
(221) ($C_{27}H_{22}N_2O$)	83.2	5.6	7.0	(391)	83.1	5.6	7.2	(391)
(222) ($C_{27}H_{20}N_2O$)	83.8	5.2	7.0	388	83.5	5.2	7.2	388
(231a) ($C_{28}H_{19}NO_3$)	80.4	4.5	3.4	417	80.6	4.6	3.4	417
(231b) ($C_{30}H_{23}NO_3$)	80.7	5.2	3.1	(446)	80.9	5.2	3.2	(446)
(231c) ($C_{30}H_{18}F_6NO_3$)				(554.1198)				(554.1191)
(230) ($C_{17}H_{13}NO_3$)	73.4	4.7	5.0	279	73.1	4.7	5.0	279
(236) ($C_{28}H_{17}NO_3$) [b]	81.2	4.3	3.3	415	81.0	4.1	3.4	415
(231e) ($C_{30}H_{23}NO_5$) [b]	75.7	4.8	2.9	(478)	75.5	4.8	2.9	(478)
($C_{30}H_{23}NO_5$) [c]				(478.1652)				(478.1655)

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy. [b] Mixture of *syn* and *anti* isomers. [c] *Anti* isomer.

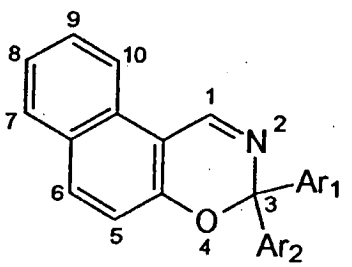
Table 8: Elemental Analysis and Mass Spectroscopic Data (contd.)

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(232a) ($C_{28}H_{19}NO$)				385.1456				385.1467
(232b) ($C_{30}H_{23}NO$)	87.2	5.8	3.2	413	87.2	5.6	3.4	413
(232c) ($C_{30}H_{17}F_6NO$)	69.3	3.3	2.5	521	69.1	3.3	2.7	521
(232e) ($C_{30}H_{23}NO_3$)	81.1	5.2	3.2	445	80.9	5.2	3.2	445
(233a) ($C_{28}H_{21}NO$)	87.1	5.7	3.5	(388)	86.8	5.4	3.6	(388)
(233b) ($C_{30}H_{25}NO$)	86.8	6.1	3.4	(416)	86.8	6.0	3.4	(416)
(234a) ($C_{29}H_{20}N_2O$)	84.3	4.9	6.5	(413)	84.5	4.9	6.8	(413)
(234b) ($C_{31}H_{24}N_2O$)	84.3	5.7	6.3	(441)	84.6	5.5	6.4	(441)
(235a) ($C_{29}H_{18}N_2O$)	85.0	4.7	6.8	410	84.9	4.4	6.8	410
(233d) ($C_{32}H_{31}N_3O$)				473.2468				473.2467
(243a) ($C_{23}H_{16}N_2O_3$)	75.1	4.4	7.7	(369)	75.0	4.4	7.6	(369)
(243b) ($C_{25}H_{20}N_2O_3$)[b]	75.4	5.1	6.9	396	75.8	5.1	7.1	396
(243b) ($C_{25}H_{20}N_2O_3$)[c]	75.8	5.2	7.0	396	75.8	5.1	7.1	396
(243c) ($C_{25}H_{20}N_2O_5$)	69.6	4.5	6.3	399 [M^+-CH=O]	70.1	4.7	6.5	428
(244a) ($C_{23}H_{16}N_2O$)	81.7	4.6	8.2	336	82.1	4.8	8.3	336
(244b) ($C_{25}H_{20}N_2O$)	82.1	5.6	7.3	(365)	82.4	5.5	7.7	(365)
(244c) ($C_{25}H_{20}N_2O_3$)	75.6	5.0	6.8	396	75.8	5.1	7.1	396
(248) ($C_{26}H_{17}NO_3$)	79.9	4.4	3.3	(392)	79.8	4.3	3.6	(392)

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy. [b] Mixture of *syn* and *anti* isomers. [c] *Anti* isomer.

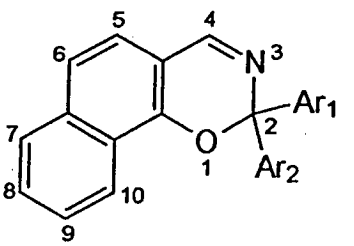
CHAPTER 3

INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2*H*-1,3-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS



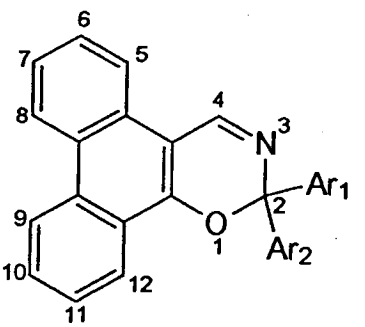
3*H*-Naphth[1,2-*e*]-1,3-oxazine

(250)



2*H*-Naphth[2,1-*e*]-1,3-oxazine

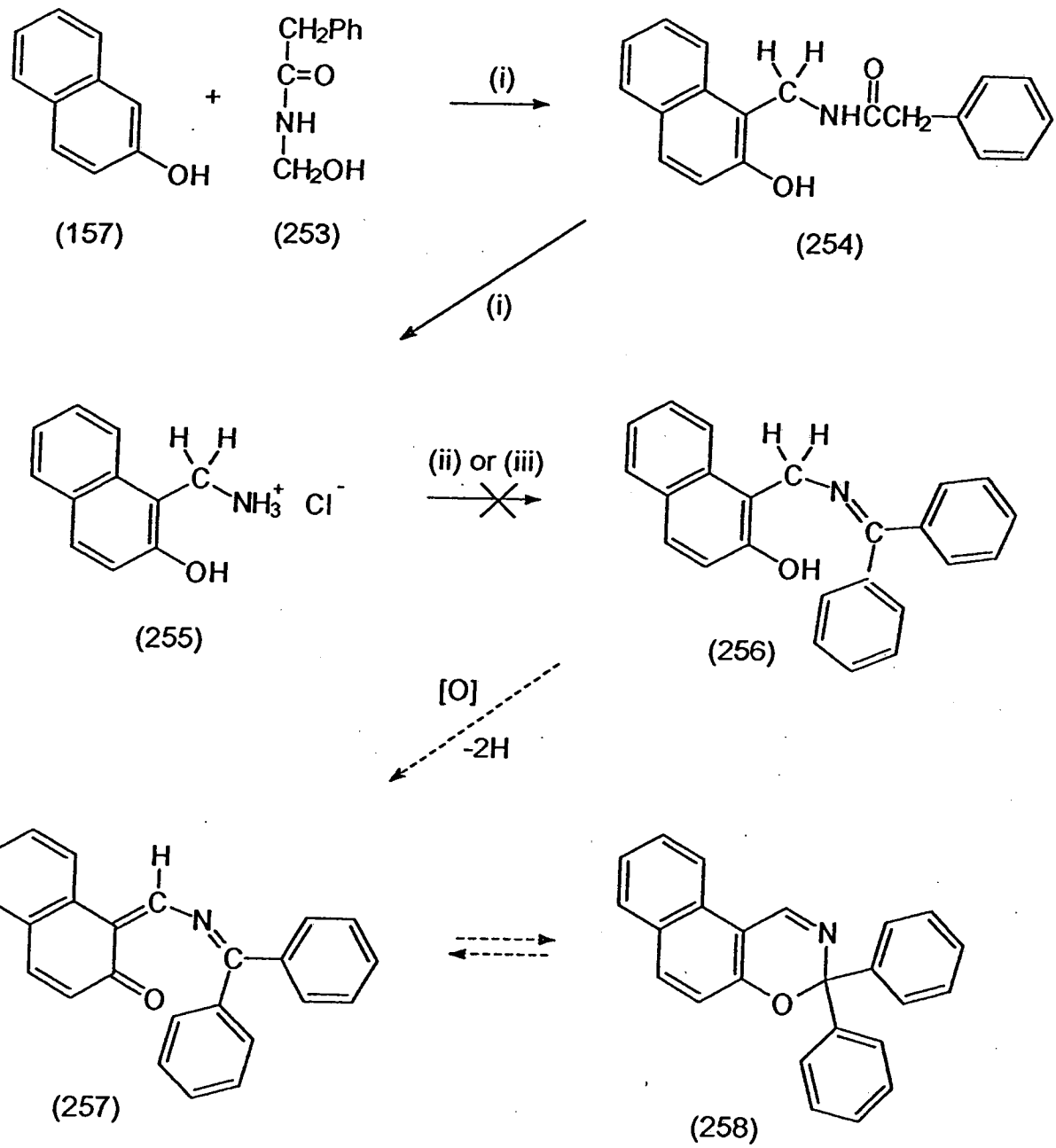
(251)



2*H*-Phenanthro[9,10-*e*]-1,3-oxazine

(252)

Scheme 60



(i) HCl (conc.), EtOH, reflux.

(ii) $Ph_2C=O$, EtOH, H_2O, reflux.

(iii) $Ph_2C=O$, Na_2CO_3, toluene, reflux (Dean and Stark).

Scheme 61

3. INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2*H*-1,3-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS

3.1 Introduction

Though fused 2,2-disubstituted 2*H*-1,3-oxazines [see Scheme 23; (104)] have obvious potential as photochromic agents, very little is known about their behaviour in this respect. Of particular interest in the current studies (Scheme 60) are 3,3-diaryl-3*H*-naphth[1,2-*e*]-1,3-oxazines (250), 2,2-diaryl-2*H*-naphth[2,1-*e*]-1,3-oxazines (251) and 2,2-diaryl-2*H*-phenanthro[9,10-*e*]-1,3-oxazines (252) which are structurally closely related to the photochromic 2,2-disubstituted fused 2*H*-1,4-oxazines [see Page 23, Scheme 23; (103)], the preparation of which was described in Chapter 2. As routes for the preparation of the disubstituted fused 2*H*-1,3-oxazines [eg (250)-(252)] have been largely unexplored in the literature, studies were undertaken to synthesise these potentially useful photochromic agents.

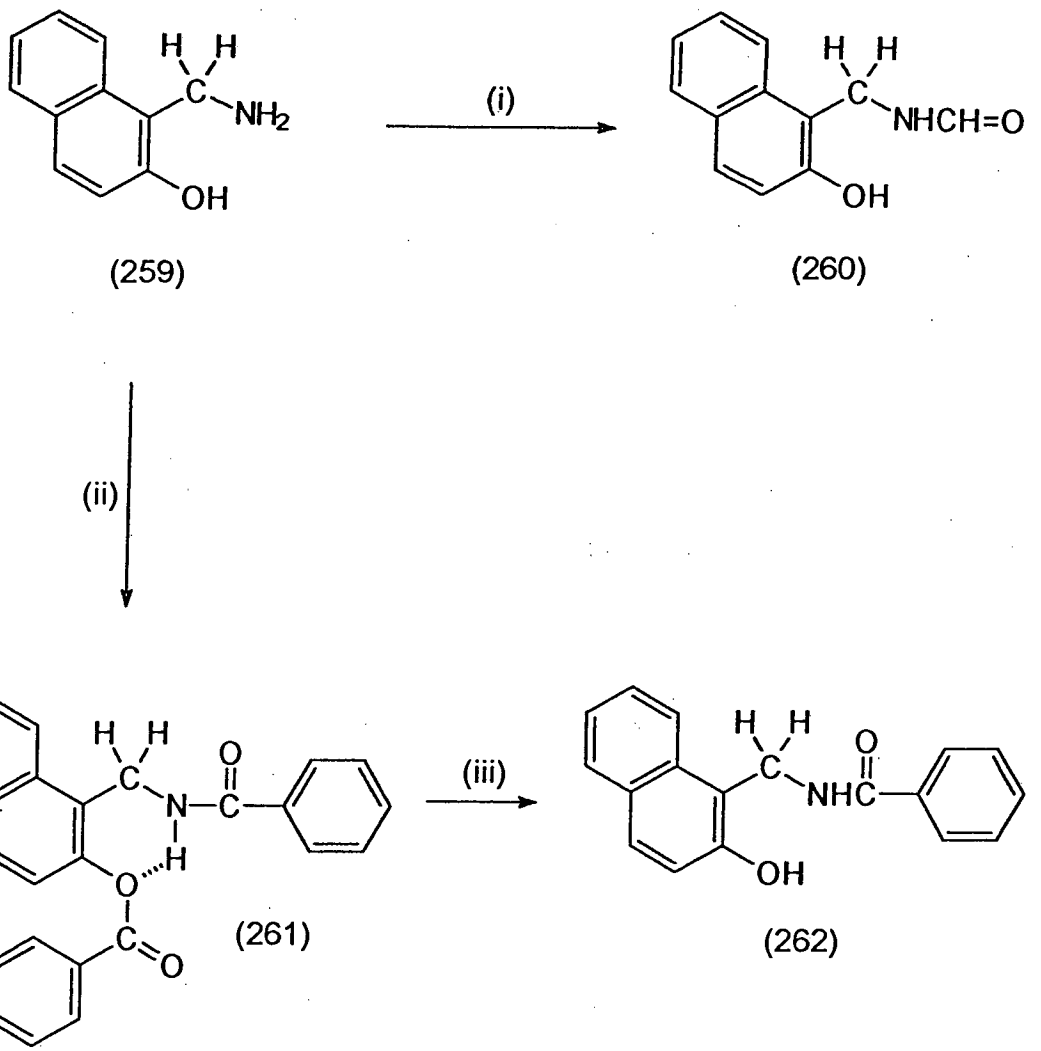
3.2 Studies on the Synthesis of 3,3-Diaryl-3*H*-naphth[1,2-*e*]-1,3-oxazine Derivatives

Initial studies under this heading centred (Scheme 61) on the known[166] three-step synthesis of the aminomethylnaphthol hydrochloride (255), the key starting material in the proposed synthetic strategy. It was hoped that the amine hydrochloride (255) would prove reactive toward diarylketones, such as

benzophenone giving the imine (256). Oxidation of the imine (256) would give the ring-opened form (257) of the desired naphthoxazine derivative (258).

Thus phenylacetamide was condensed with formaldehyde in aqueous sodium carbonate solution to give *N*-(hydroxymethyl)phenylacetamide (253) in good yield (71%). In turn, reaction of the amide (253) with 2-naphthol (157) under reflux in ethanol in the presence of concentrated hydrochloric acid gave a good yield (75%) of the 1-phenylacetamidomethyl-2-naphthol (254). Further heating of the naphthylmethylamide (254) with concentrated hydrochloric acid in ethanol afforded the known[166] aminomethylnaphthol hydrochloride (255) in excellent yield (90%). The structure of (255) is supported by its mass, ir and ^{1}H nmr spectra.

The reaction of the aminomethylnaphthol hydrochloride (255) with benzophenone was next investigated. However, reaction in refluxing aqueous ethanol yielded none of the desired imine (256) and the amine hydrochloride (255) was recovered in high yield (71%). In an alternative approach, neutralisation of the amine hydrochloride (255) and its reaction with benzophenone was attempted as a 'one-pot' procedure. A mixture of the hydrochloride (255), benzophenone and sodium carbonate was heated in toluene with azeotropic removal of water using a Dean and Stark apparatus. However, a multicomponent gum was isolated from this reaction, from which none of the imine (256) could be obtained.

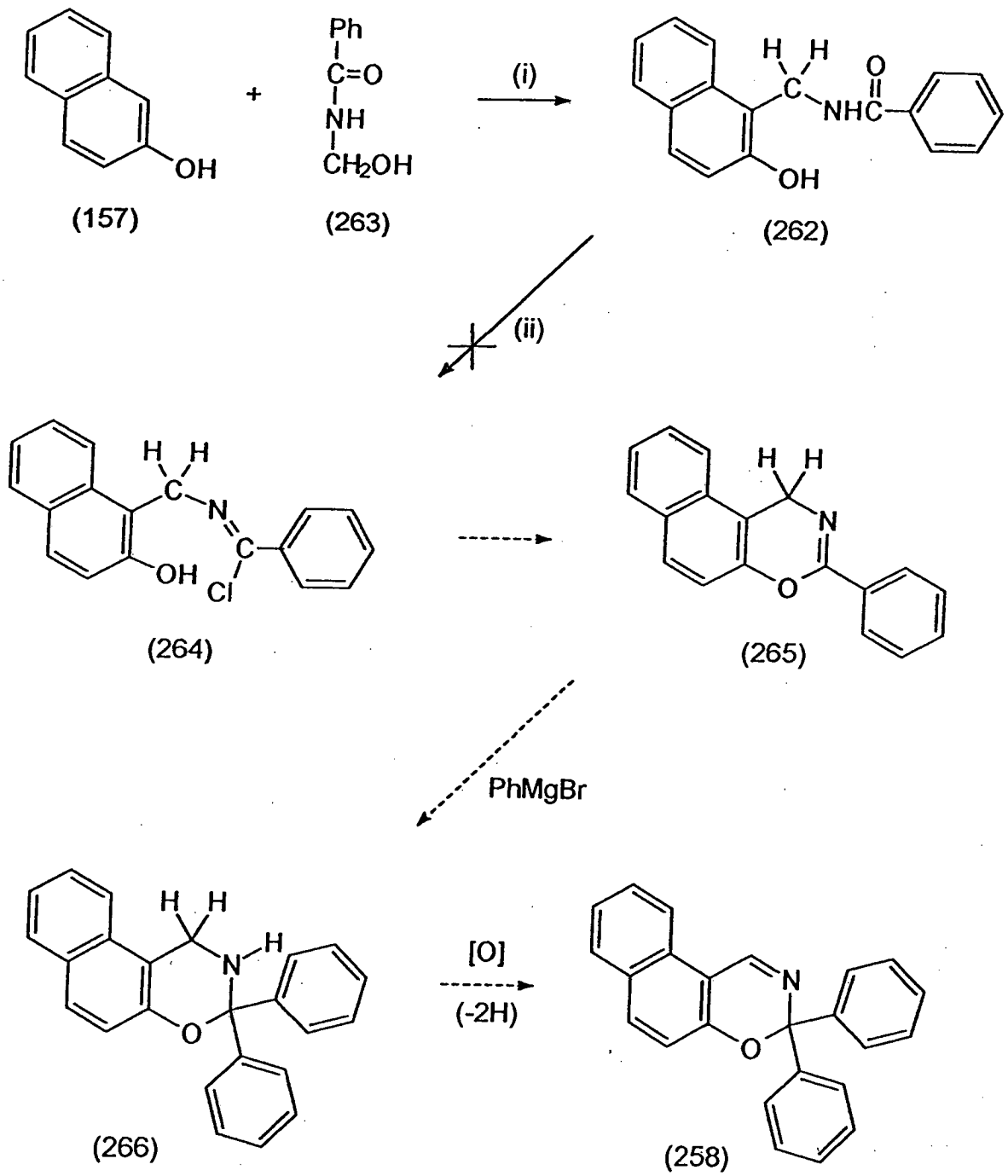


(i) HCO_2Bu^n, reflux.

(ii) PhCOCl, Et_3N, dioxane, room temp.

(iii) Na_2CO_3, H_2O, EtOH, reflux.

Scheme 62



(i) HCl (conc.), EtOH, reflux.

(ii) $POCl_3$, Pr^i_2NEt, CH_2Cl_2, 0°C to room temp.

Scheme 63

Due to the disinclination of the amine hydrochloride (255) to react with benzophenone, alternative strategies for the synthesis of the naphth-1,3-oxazine derivative (258) were investigated. It was hoped that the aminomethylnaphthol hydrochloride (255) could be neutralised (Scheme 62) to give the known[166] but poorly documented 1-aminomethyl-2-naphthol (259). It was further hoped that preparation of the dibenzoyl derivative (261) followed by selective hydrolysis of the ester functionality would afford the amide (262). Preparation of the amide (262) would allow attempts to be made (Scheme 63) to achieve its chlorination [(262)→(264)] and subsequent cyclisation to the naphth-1,3-oxazine derivative (265). Reaction of (265) with Grignard reagents such as phenylmagnesium bromide could afford the 1,2-dihydro derivative (266) of the desired diphenylnaphthoxazine derivative (258).

Preparation (Scheme 62) of the aminomethylnaphthol (259) was therefore attempted by neutralisation of an aqueous solution of its hydrochloride salt [Scheme 61; (255)] with sodium acetate at 50°C. Though the crude product so obtained gave a mass spectrum indicating that it contained the desired aminomethylnaphthol (259), attempts to purify this product were unsuccessful and neither combustion analysis nor nmr spectra consistent with the structure of the aminomethylnaphthol (259) could be obtained.

It was decided (Scheme 62) to prepare a simple derivative of the aminomethylnaphthol (259) which it was hoped would be more easily purified. In an attempt to prepare the formamide derivative (260), the crude

aminomethylnaphthol (259) was heated with formic acid. Unfortunately, only an intractable solid was obtained from this reaction. In a similar experiment, the crude amine (259) was heated with *n*-butyl formate giving a poor yield (22%) of a cream solid product which gave analytical and spectroscopic data consistent with its formulation as the formamide derivative (260). The ir spectrum of the formamide derivative (260) contains a sharp NH absorption band (ν_{max} 3310cm^{-1}), a broad OH absorption (ν_{max} 3300-2800 cm^{-1}) and a band corresponding to the amide carbonyl group (ν_{max} 1628 cm^{-1}). The ^{1}H nmr spectrum shows a singlet at δ_H 9.34 due to the hydroxyl group and a broad singlet (δ_H 6.75-6.55) corresponding to the amido hydrogen. Only the former is completely removed on contact with deuterium oxide. Also present in the ^{1}H nmr spectrum is the proton of the formyl moiety (δ_H 8.17) as well as signals due to the naphthalene and methylene hydrogens.

While the isolation of the formamide derivative (260) confirms that the crude starting material did contain the aminomethylnaphthol (259) the poor yield in which it was isolated was of concern. Nevertheless it was decided to attempt the preparation of the required dibenzoyl derivative (261) as the efficiency of this reaction would provide further evidence for the composition of the crude hydroxy-amine (259). Thus, a 1,4-dioxane solution of the crude aminomethyl-naphthol (259) was treated at room temperature with triethylamine and two equivalents of benzoyl chloride. Under these conditions a poor yield (27%) of the dibenzoyl compound (261) was isolated, which gave analytical and spectroscopic properties consistent with its assigned structure. The ^{1}H nmr

spectrum shows in addition to signals due to the aromatic protons, a two-proton doublet (δ_H 4.93) due to the methylene group and a one-proton triplet (δ_H 8.83) due to the amido proton. The resistance of the latter to exchange with deuterium oxide may be due to an intramolecular hydrogen bond with the ester oxygen as shown (261). To exclude the possibility of the inefficiency in the dibenzoylation of the aminomethylnaphthol (259) being due to the use of an insufficient amount of benzoyl chloride, the reaction was repeated using four equivalents of the acid chloride. However, reaction in the presence of triethylamine in 1,4-dioxane again gave a poor yield (26%) of the dibenzoyl compound (261). Though the formation of the dibenzoyl derivative (261) further supports the structure of the aminomethylnaphthol (259), the poor yield (27%) of this reaction, which is commensurate with the yield (22%) of the formylation reaction [(259)→(260)], suggests that the aminomethylnaphthol (259) is very impure.

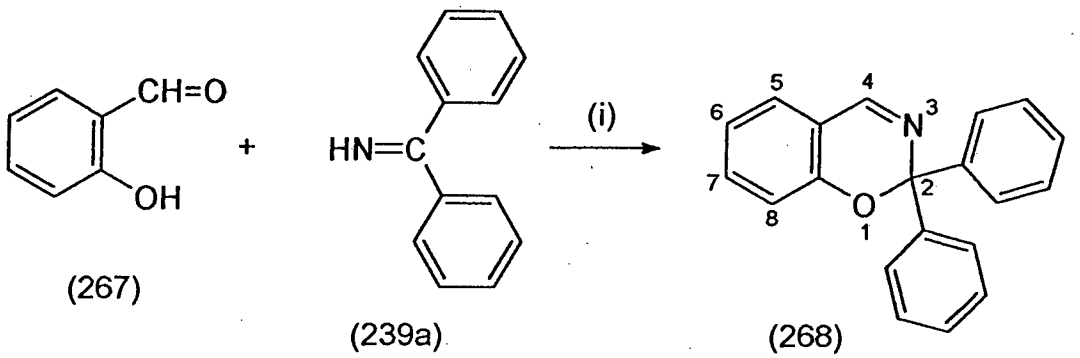
With the dibenzoyl derivative (261) to hand, hydrolysis of its ester functionality was attempted. Treatment of an ethanol solution of the dibenzoyl derivative (261) with aqueous sodium carbonate gave an excellent yield (92%) of a product whose analytical and spectroscopic properties were fully in accord with its formulation as the 1-benzoylaminomethyl-2-naphthol (262).

As previously mentioned, the stimulus for the synthesis of 1-benzoylaminomethyl-2-naphthol (262) was desired to allow (Scheme 63) of its conversion to the iminochloride (264) and subsequent cyclisation to be studied.

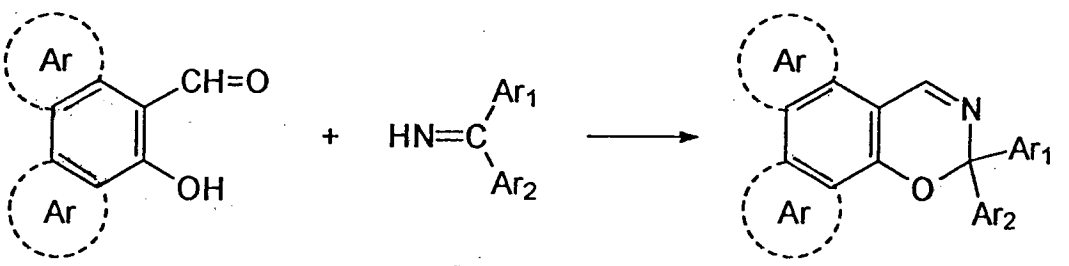
In order to facilitate these investigations, the re-preparation of the *N*-benzoyl compound (262) was required. Having previously (Scheme 61 and 62) prepared the 1-benzoylaminomethyl-2-naphthol (262) in six steps including the problematic conversion of the 1-aminomethyl-2-naphthol hydrochloride (255) to the free amine (259), a more straightforward synthesis was sought. As the synthesis of 1-phenylacetamidomethyl-2-naphthol (254) was achieved by the acid catalysed reaction of *N*-(hydroxymethyl)phenylacetamide (253) with 2-naphthol (157), it was expected that the preparation (Scheme 63) of 1-benzoylaminomethyl-2-naphthol (262) could be achieved by the analogous reaction of the known[167] *N*-(hydroxymethyl)benzamide (263) with 2-naphthol (157).

In practice, *N*-(hydroxymethyl)benzamide (263) was prepared in excellent yield (86%) by condensation of benzamide with formaldehyde in aqueous potassium carbonate. The hydroxymethylbenzamide (263) reacted as predicted with 2-naphthol (157) under reflux in ethanol in the presence of concentrated hydrochloric acid, giving 1-benzoylaminomethyl-2-naphthol (262) in excellent yield (84%).

With the 1-benzoylaminomethyl-2-naphthol (262) now readily available, its chlorination was attempted. Unfortunately, reaction of (262) with phosphorus oxychloride in the presence of diisopropylethylamine at 0-5°C in dichloromethane gave only intractable solids and gums.



(267) (239a) (268)

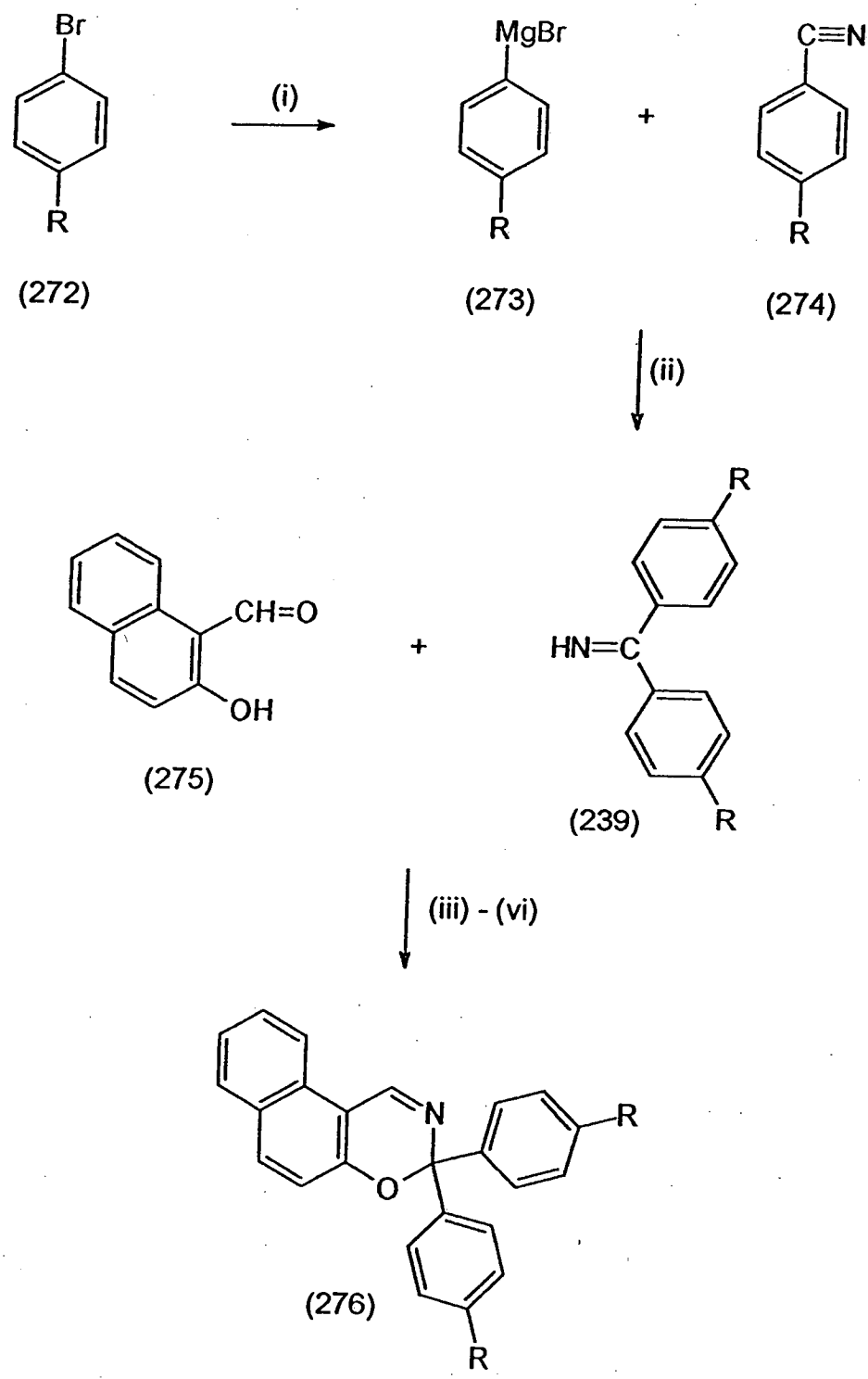


(269) (270) (271)

(Ar = aromatic nucleus)

(i) Et_3N, benzene, reflux.

Scheme 64



(i) Mg, ether, reflux.

(ii) ether, reflux.

(iii) Et_3N, toluene, reflux.

(iv) ptsa, toluene, reflux (Dean and Stark).

(v) 4A sieves, toluene, reflux (Dean and Stark).

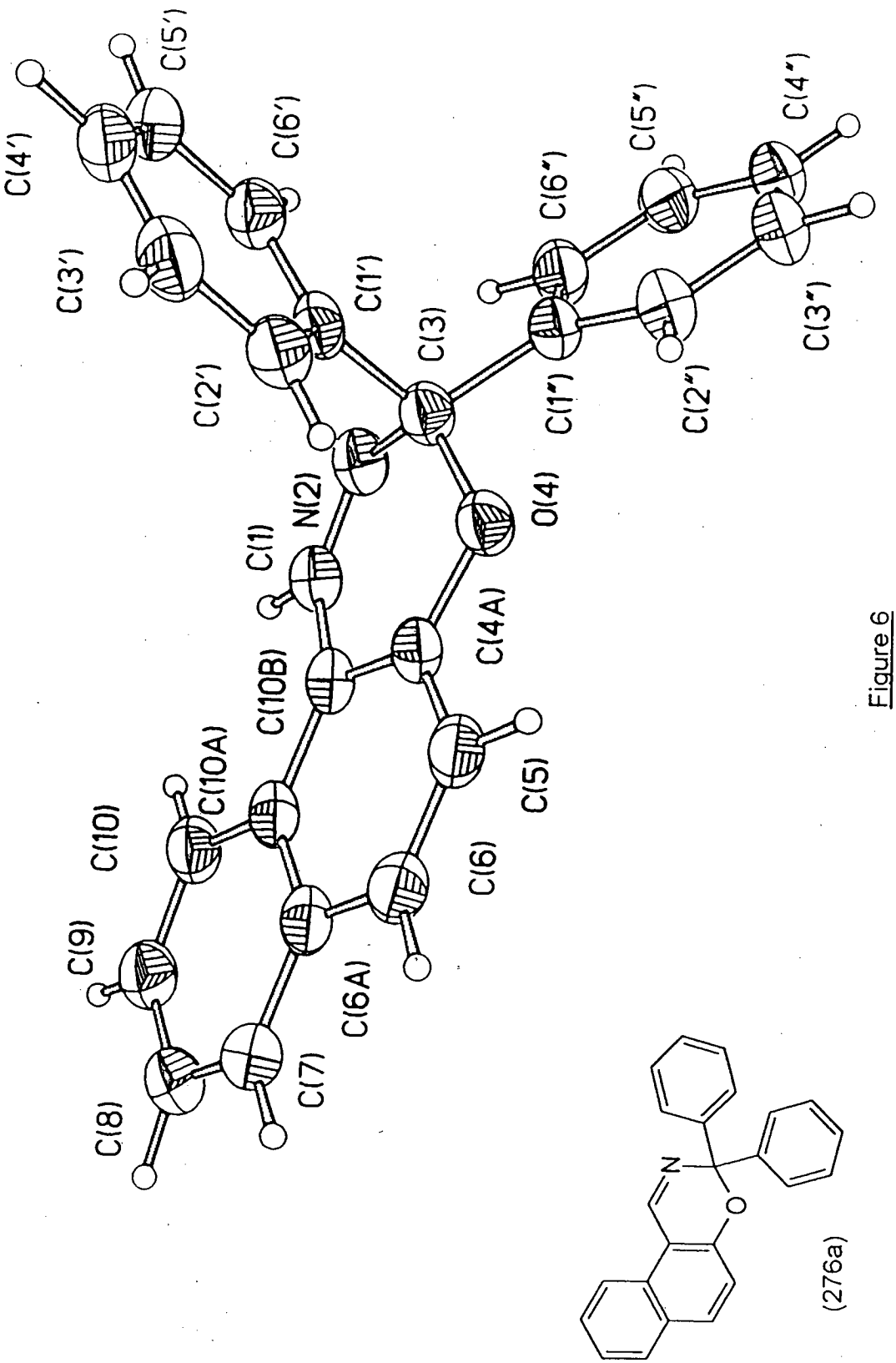
(vi) ptsa, 4A sieves, toluene, reflux (Dean and Stark).

R
a; H
b; Me
c; OMe
d; NMe_2

Scheme 65

During the foregoing studies an alternative strategy for the preparation of the naphthoxazine derivative (258) was developed. A literature search revealed a paper[168] in which (Scheme 64) the preparation of 2,2-diphenyl-2*H*-benz-1,3-oxazine (268) is described by the reaction of diphenylketimine (239a) with salicylaldehyde (267) in the presence of triethylamine. It was thought likely that the analogous reaction (Scheme 65) of diphenylketimine (239a) with the commercially available 2-hydroxy-1-naphthaldehyde (275) would afford the desired naphthoxazine derivative (276a). This synthetic route was attractive as there was thought to be considerable scope for the synthesis (Scheme 64) of other fused 2,2-disubstituted 2*H*-1,3-oxazine derivatives (271) using the same methodology. That is, investigations could be made on the availability of other ketimine derivatives (270) and polyaromatic hydroxy-aldehydes (269) for use as starting materials in such syntheses.

Thus (Scheme 65) diphenylketimine (239a) was prepared[169,170] in good yield (63%) by the reaction of benzonitrile (274a) with phenylmagnesium bromide (273a) under reflux in ether. The imine (239a) was reacted with 2-hydroxy-1-naphthaldehyde (275) in the presence of triethylamine in refluxing toluene for 6 h. The product isolated in good yield (72%) from this reaction gave mass, ir and ^{1}H nmr spectra consistent with it being the desired naphthoxazine derivative (276a). The ir spectrum shows an imine absorption band (ν_{max} 1640 cm^{-1}) while the ^{1}H nmr spectrum shows a one-proton singlet due to the imine hydrogen (δ_H 9.10) and multiplets due to the aromatic protons. The uv/visible



(276a)

Figure 6

X-Ray Diffraction Data for 3,3-Diphenyl-3*H*-naphth[1,2-e]-1,3-oxazine (276a)

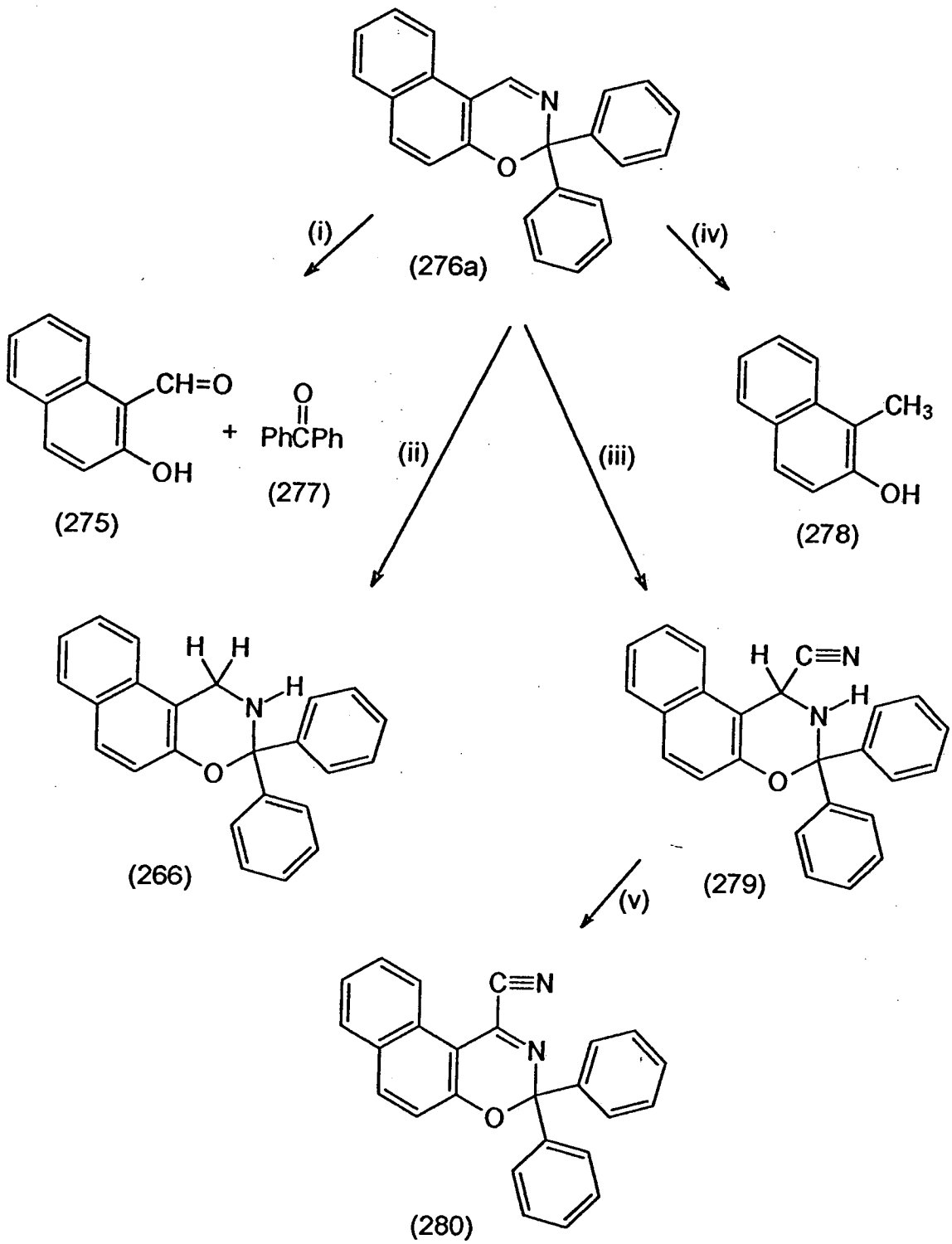
Table 9: Bond Lengths (Angstroms) with Standard Deviations

C(1)-N(2)	1.279(4)	C(10A)-C(10B)	1.437(4)
C(1)-C(10B)	1.452(4)	C(1')-C(2')	1.390(5)
C(1)-H(1)	1.02(4)	C(1')-C(6')	1.394(4)
N(2)-C(3)	1.460(4)	C(2')-C(3')	1.389(5)
C(3)-0(4)	1.454(3)	C(2')-H(3')	0.99(4)
C(3)-C(1')	1.529(4)	C(3')-C(4')	1.372(6)
C(3)-C(1")	1.535(4)	C(3')-H(4')	1.01(4)
0(4)-C(4A)	1.365(3)	C(4')-C(5')	1.387(6)
C(4A)-C(10B)	1.376(4)	C(4')-H(4')	1.01(4)
C(4A)-C(5)	1.403(4)	C(5')-C(6')	1.386(5)
C(5)-C(6)	1.362(4)	C(5')-H(5')	0.97(4)
C(5)-H(5)	1.01(4)	C(6')-H(6')	1.03(4)
C(6)-C(6A)	1.421(5)	C(1")-C(6")	1.381(5)
C(6)-H(6)	0.99(4)	C(1")-C(2")	1.397(5)
C(6A)-C(7)	1.410(4)	C(2")-C(3")	1.385(5)
C(6A)-C(10A)	1.424(4)	C(2")-H(2")	0.92(4)
C(7)-C(8)	1.369(5)	C(3")-C(4")	1.385(6)
C(7)-H(7)	0.96(4)	C(3")-H(3")	0.97(4)
C(8)-C(9)	1.406(5)	C(4")-C(5")	1.385(5)
C(9)-C(10)	1.368(5)	C(4")-H(4")	0.96(4)
C(8)-H(8)	0.99(4)	C(5")-C(5")	1.393(4)
C(9)-H(9)	1.03(5)	C(5")-H(5")	0.99(4)
C(10)-C(10A)	1.414(4)	C(6")-H(6")	0.94(4)
C(10)-H(10)	0.94(4)		

X-Ray Diffraction Data for 3,3-Diphenyl-3*H*-naphth[1,2-e]-1,3-oxazine (276a)

Table 10: Bond Angles (Degrees) with Standard Deviations

N(2)-C(1)-C(10B)	124.9(3)	C(4A)-C(10B)-C(10A)	116.0(3)
N(2)-C(1)-H(1)	119.4(19)	C(10A)-C(10B)-C(1)	124.5(3)
C(10B)-C(1)-H(1)	115.7(19)	C(2')-C(1')-C(6')	118.8(3)
C(1)-N(2)-C(3)	118.2(3)	C(2')-C(1')-C(3)	121.6(3)
0(4)-C(3)-N(2)	114.7(2)	C(6')-C(1')-C(3)	119.6(3)
0(4)-C(3)-C(1')	109.8(2)	C(3')-C(2')-C(1')	119.8(3)
N(2)-C(3)-C(1')	108.0(2)	C(3')-C(2')-H(2')	117(2)
0(4)-C(3)-C(1")	104.2(2)	C(1')-C(2')-H(2')	123(2)
N(2)-C(3)-C(1")	109.3(3)	C(4')-C(3')-C(2')	121.3(4)
C(1')-C(3)-C(1")	110.8(2)	C(4')-C(3')-H(3')	121(2)
C(4A)-0(4)-C(3)	118.3(2)	C(2')-C(3')-H(3')	118(2)
0(4)-C(4A)-C(10B)	121.2(3)	C(3')-C(4')-C(5')	119.3(3)
0(4)-C(4A)-C(5)	116.1(3)	C(3')-C(4')-H(4')	118(2)
C(10B)-C(4A)-C(5)	122.5(3)	C(5')-C(4')-H(4')	123(2)
C(6)-C(5)-C(4A)	118.9(3)	C(6')-C(5')-C(4')	120.0(4)
C(6)-C(5)-H(5)	123(2)	C(6')-C(5')-H(5')	118(3)
C(4A)-C(5)-H(5)	118(2)	C(4')-C(5')-H(5')	122(3)
C(5)-C(6)-C(6A)	121.7(3)	C(5')-C(6')-C(1')	120.7(3)
C(5)-C(6)-H(6)	120(2)	C(5')-C(6')-H(6')	121(2)
C(6A)-C(6)-H(6)	118(2)	C(1')-C(6')-H(6')	118(2)
C(7)-C(6A)-C(6)	121.1(3)	C(6")-C(1")-C-(2")	119.1(3)
C(7)-C(6A)-C(10A)	119.7(3)	C(6")-C(1")-C(3)	121.8(3)
C(6)-C(W-C(10A)	119.2(3)	C(2")-C(1")-C(3)	119.1(3)
C(8)-C(7)-C(6A)	120.9(3)	C(3")-C(2")-C(1")	120.3(3)
C(8)-C(7)-H(7)	120(2)	C(3")-C(2")-H(2")	119(2)
C(6A)-C(7)-H(7)	119(2)	C(1")-C(2")-H(2")	121(2)
C(7)-C(8)-C(9)	119.6(3)	C(4")-C(3")-C(2")	120.5(3)
C(7)-C(8)-H(8)	117(2)	C(4")-C(3")-H(3")	119(2)
C(9)-C(8)-H(8)	124(2)	C(2")-C(3")-H(3")	121(2)
C(10)-C(9)-C(8)	120.7(3)	C(3")-C(4")-C(5")	119.3(3)
C(10)-C(9)-H(9)	120(2)	C(3")-C(4")-H(4")	127(2)
C(8)-C(9)-H(9)	119(2)	C(5")-C(4")-H(4")	114(2)
C(9)-C(10)-C(10A)	121.3(3)	C(4")-C(5")-C(6")	120.3(4)
C(9)-C(10)-H(10)	120(2)	C(4")-C(5")-H(5")	117(2)
C(10A)-C(10)-H(10)	119(2)	C(6")-C(5")-H(5")	122(2)
C(10)-C(10A)-C(6A)	117.8(3)	C(1")-C(6")-C(5")	120.5(3)
C(10)-C(10A)-C(10B)	123.8(3)	C(1")-C(6")-H(6")	117(2)
C(6A)-C(10A)-C(10B)	118.4(3)	C(5")-C(6")-H(6")	123(2)
C(4A)-C(10B)-C(I0A)	119.3(3)		



(i) HCl(aqu.), EtOH, reflux.

(ii) $NaBH_4$, H_2O, DME, room temp.

(iii) KCN, AcOH, room temp.

(iv) H_2, Pd-C, dioxane, room temp., atmos. press.

(v) MnO_2, DME, room temp.

Scheme 66

spectrum of the diphenylnaphthoxazine derivative (276a) and that of each of the fused 1,3-oxazine derivatives prepared in these studies is described later in this chapter (see Section 3.5, Page 278). At this point a crystal of (276a) was sent for X-ray diffraction analysis (see Page 263, Figure 6). The relevant bond lengths and bond angles are shown in Tables 9 and 10.

With the diphenylnaphthoxazine derivative (276a) to hand, work was undertaken to further support its structure with an investigation (Scheme 66) of its chemical behaviour as a cyclic imine. With this aim, the hydrolysis of the diphenylnaphthoxazine derivative (276a) was attempted by treatment with aqueous hydrochloric acid at room temperature in ethanol. Under these conditions the naphthoxazine ring was completely hydrolysed giving a poor yield (32%) of 2-hydroxy-1-naphthaldehyde (275) and a quantitative yield of benzophenone (277).

The preparation of the 1,2-dihydro derivative (266) of the diphenylnaphthoxazine (276a) was attempted through hydrogenation at room temperature atmospheric pressure over palladium-on-charcoal. However, the product of this reaction, isolated in high yield (85%) gave analytical and spectroscopic data consistent with it being 1-methyl-2-naphthol (278). No other product was isolated from this reaction. In a further attempt to prepare the dihydro derivative (266), the naphthoxazine derivative (276a) was treated with sodium borohydride at room temperature in aqueous 1,2-dimethoxyethane. Even after a prolonged period under these conditions the

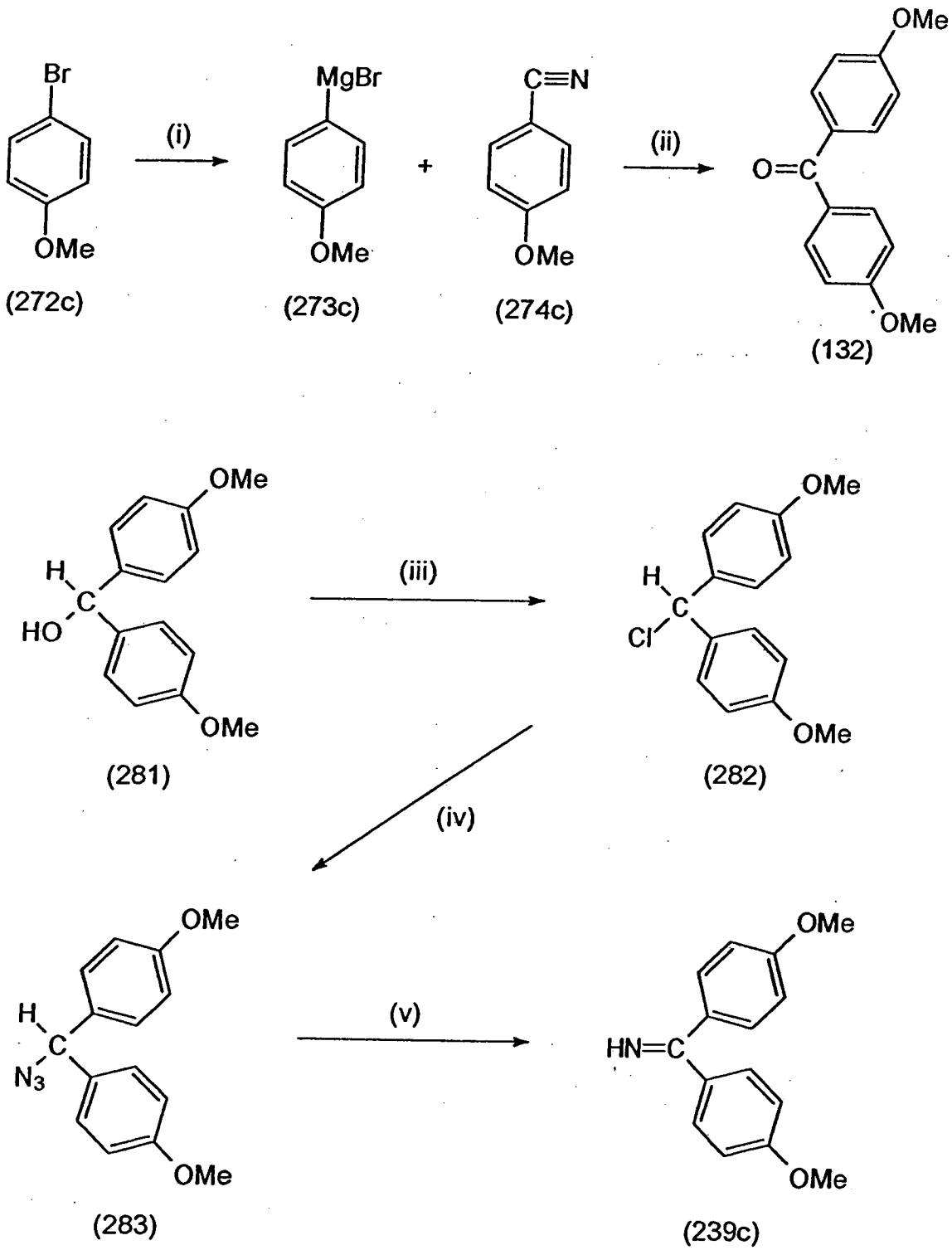
unreacted naphthoxazine derivative (276a) was recovered in moderate yield (39%) together with a small amount (7%) of a product whose analytical and mass spectral data are fully in accord with its formulation as the dihydro compound (266). However, the ^1H nmr spectrum contains certain unusual features. The methylene group gives rise to two one-proton doublets with vastly different chemical shifts (δ_H 9.04 and 5.81). The variation in these chemical shifts suggests that one of the protons is experiencing a much greater degree of shielding than the other. It is likely that the origin of this phenomenon lies in the non-planarity of the oxazine ring. The twisted shape of the reduced oxazine ring results in one of the methylene hydrogens being in the plane of the naphthalene rings while the other is in an axial position. The axial proton is shielded by the ring current of the naphthalene nucleus and consequently gives a signal at significantly lower frequency than the equatorial proton.

The addition of hydrogen cyanide across the imino double bond was also attempted. The reaction of the diphenylnaphthoxazine derivative (276a) with potassium cyanide in glacial acetic acid at room temperature gave a good yield (66%) of a colourless solid product whose analytical and spectroscopic properties support its formulation as the 1-cyano-1,2-dihydronaphthoxazine derivative (279).

In further support of the structure of the cyanodihydro compound (279) its oxidation to the cyanonaphthoxazine derivative (280) was attempted using

manganese dioxide at room temperature in 1,2-dimethoxyethane. Under these conditions the desired cyanonaphthoxazine derivative (280) was isolated in moderate yield (58%) and was characterised by its analytical and spectroscopic properties.

Having established (Scheme 65) that the methodology reported in the literature[168] can be used for the synthesis of the naphth-1,3-oxazine derivative (276a) the preparation of further 3,3-diaryl-3*H*-naphth[1,2-*e*]-1,3-oxazines (276) was desirable. However, prior to attempts to apply this methodology to the synthesis of other naphthoxazine derivatives, work was undertaken to optimise the reaction conditions based on the preparation of the diphenyl compound (276a). Initially, the reaction conditions used previously for the synthesis of the diphenylnaphthoxazine derivative (276a) were repeated and the reaction time extended. 2-Hydroxy-1-naphthaldehyde (275) was reacted with diphenyl-ketimine (239a) in the presence of triethylamine in refluxing toluene for 14 h and gave an improved yield (82%) of the naphthoxazine derivative (276a). In an alternative approach the hydroxy-aldehyde (275) and the ketimine (239a) were heated in the presence of toluene-4-sulphonic acid in toluene using a Dean and Stark apparatus to azeotropically remove water. However, under these conditions only a moderate yield (51%) of the naphthoxazine derivative (276a) was isolated. Reaction of the hydroxy-aldehyde (275) and the ketimine (239a) was also attempted in refluxing toluene in the presence of 4Å molecular sieves but again gave only a moderate yield (51%) of the desired naphthoxazine derivative (276). In a further experiment using 4Å sieves,



(i) Mg, ether, reflux.

(ii) ether, reflux.

(iii) HCl(g), $CaCl_2$, ether, 0°C to room temp.

(iv) NaN_3, DMF, room temp.

(v) xylene, reflux.

Scheme 67

toluene-4-sulphonic acid and a Dean and Stark apparatus, the product (276a) was isolated in good yield (64%). The yield of naphthoxazine derivative (276a) isolated in the foregoing studies is significantly lower than previously achieved when the reaction was performed in refluxing toluene in the presence of triethylamine. Consequently the next attempted synthesis, that of 3,3-di-(4-methylphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276b) was carried out using the latter conditions.

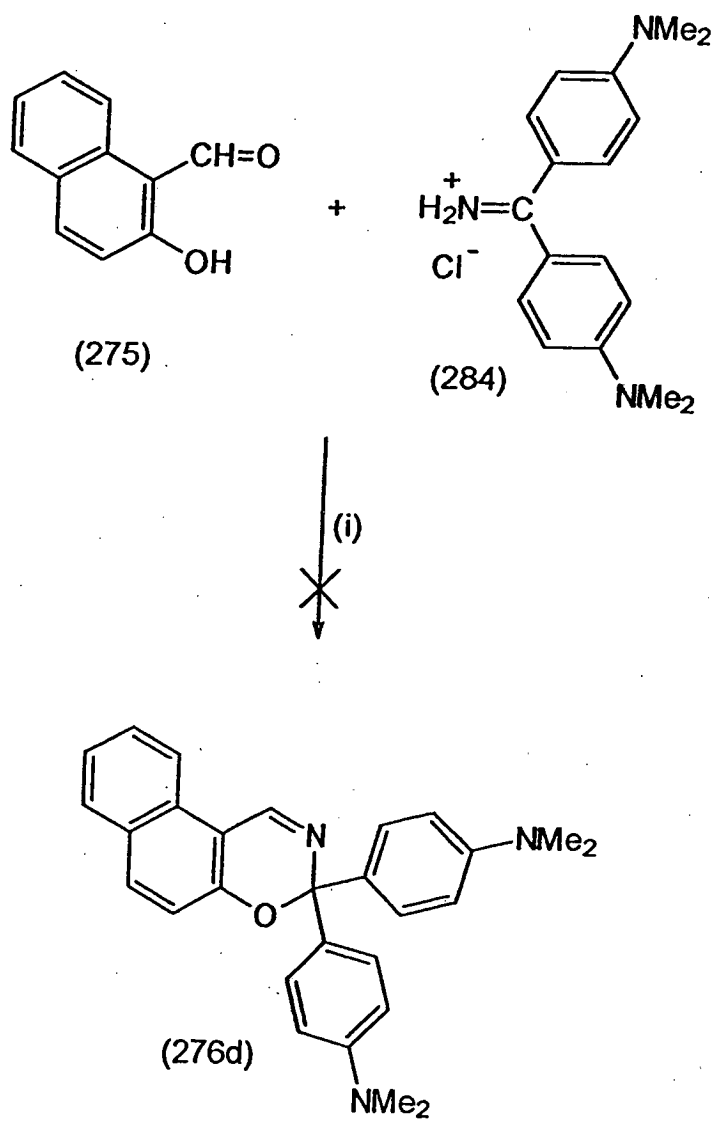
Preparation of the known[169-171] di-(4-methylphenyl)ketimine (239b) was required to facilitate the synthesis of 3,3-di-(4-methylphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276b). Treatment of 4-bromotoluene (272b) with magnesium in refluxing ether followed by further heating with 4-methylbenzonitrile (274b) gave a moderate yield (58%) of the imine (239b) whose analytical and spectroscopic properties were fully in accord with its assigned structure. The reaction of the imine (239b) with 2-hydroxy-1-naphthaldehyde (275) in the presence of triethylamine under reflux in toluene gave an excellent yield (83%) of the desired di-(4-methylphenyl)naphthoxazine derivative (276b).

In order to attempt the analogous synthesis of 3,3-di-(4-methoxyphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276c), work was started on the preparation of the required di-(4-methoxyphenyl)ketimine (239c). However (Scheme 67), reaction of commercially available 4-methoxybenzonitrile (274c) with 4-methoxyphenylmagnesium bromide (273c) afforded none of the desired imine (239c). Reaction under these conditions gave a mixture from which

methoxybenzene and 4-methoxybenzonitrile (274c) were both isolated in poor yield (23%) yield together with a small amount (14%) of 4,4'-dimethoxy-benzophenone (132).

An alternative strategy for the synthesis of di-(4-methoxyphenyl)ketimine (239c) was evidently necessary. Commercially available di-(4-methoxyphenyl)-methanol (281) is known[148] to be converted to the chloro compound (282) on treatment with hydrogen chloride gas. It was hoped that reaction of the chloro compound (282) with sodium azide would afford di-(4-methoxyphenyl)methyl azide (283), thermolysis of which would give the imine (239c). In practice, the chloro compound (282) was obtained in excellent yield (91%) by treatment of an ether solution of the benzhydrol derivative (281) with hydrogen chloride gas in the presence of calcium chloride at 0°C to room temperature. Treatment of the chloro compound (282) with sodium azide at room temperature in dimethylformamide gave a quantitative yield of a cream solid whose mass and ir spectra support its formulation as the azide (283). Prolonged heating of the azide (283) under reflux in xylene gave a poor yield (41%) of di-(4-methoxyphenyl)ketimine (239c).

With the di-(4-methoxyphenyl)ketimine (239c) now available, its reaction (Scheme 65) with 2-hydroxy-1-naphthaldehyde (275) was studied. A toluene solution of the hydroxy-aldehyde (275) the ketimine (239c) and triethylamine was heated under reflux. Under these conditions no reaction occurred and the ketimine (239c) was recovered in high yield (75%). In an alternative approach,



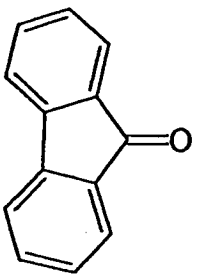
(i) Et_3N, toluene, reflux.

Scheme 68

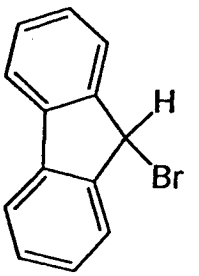
the hydroxy-aldehyde (275) and the ketimine (239c) were heated in the presence of toluene-4-sulphonic acid in toluene using a Dean and Stark apparatus to remove water. While these conditions had previously proved suitable for the synthesis of the parent diphenylnaphthoxazine derivative (276a), none of the desired di-(4-methoxyphenyl) compound (276c) was isolated and the hydroxy-aldehyde (275) was recovered in moderate yield (56%).

It is disappointing that the di-(4-methoxyphenyl)naphthoxazine derivative (276c) could not be prepared by the foregoing methodology. The likely mechanism of the formation of the naphth-1,3-oxazines [eg (276a)] prepared in toluene in the presence of triethylamine begins with deprotonation of the hydroxyl group of (275) by triethylamine then nucleophilic attack by the naphthoxide ion on the imine (239a). As the di-(4-methoxyphenyl)ketimine (239c) is likely to be more electron-rich than both the diphenyl (239a) and the di-(4-methylphenyl) (239b) ketimines, this nucleophilic attack may be less favourable. The same rationale can also be applied to the failure of this reaction under acid catalysis. Due to a lack of time, studies on the synthesis of the di-(4-methoxyphenyl)naphth-oxazine derivative (276c) were terminated at this point.

Studies on the synthesis of 3,3-di-(4-*N,N*-dimethylaminophenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276d) did not require the preparation of the ketimine (239d) as (Scheme 68) di-(4-*N,N*-dimethylaminophenyl)ketimine hydrochloride (284) is commercially available as auramine hydrochloride. 2-Hydroxy-1-naphth-



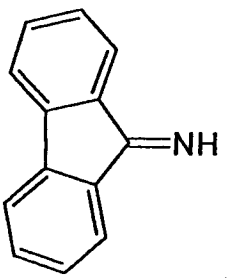
(285)



(286)

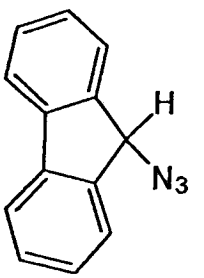
(i)

(ii)



(287)

(iii)



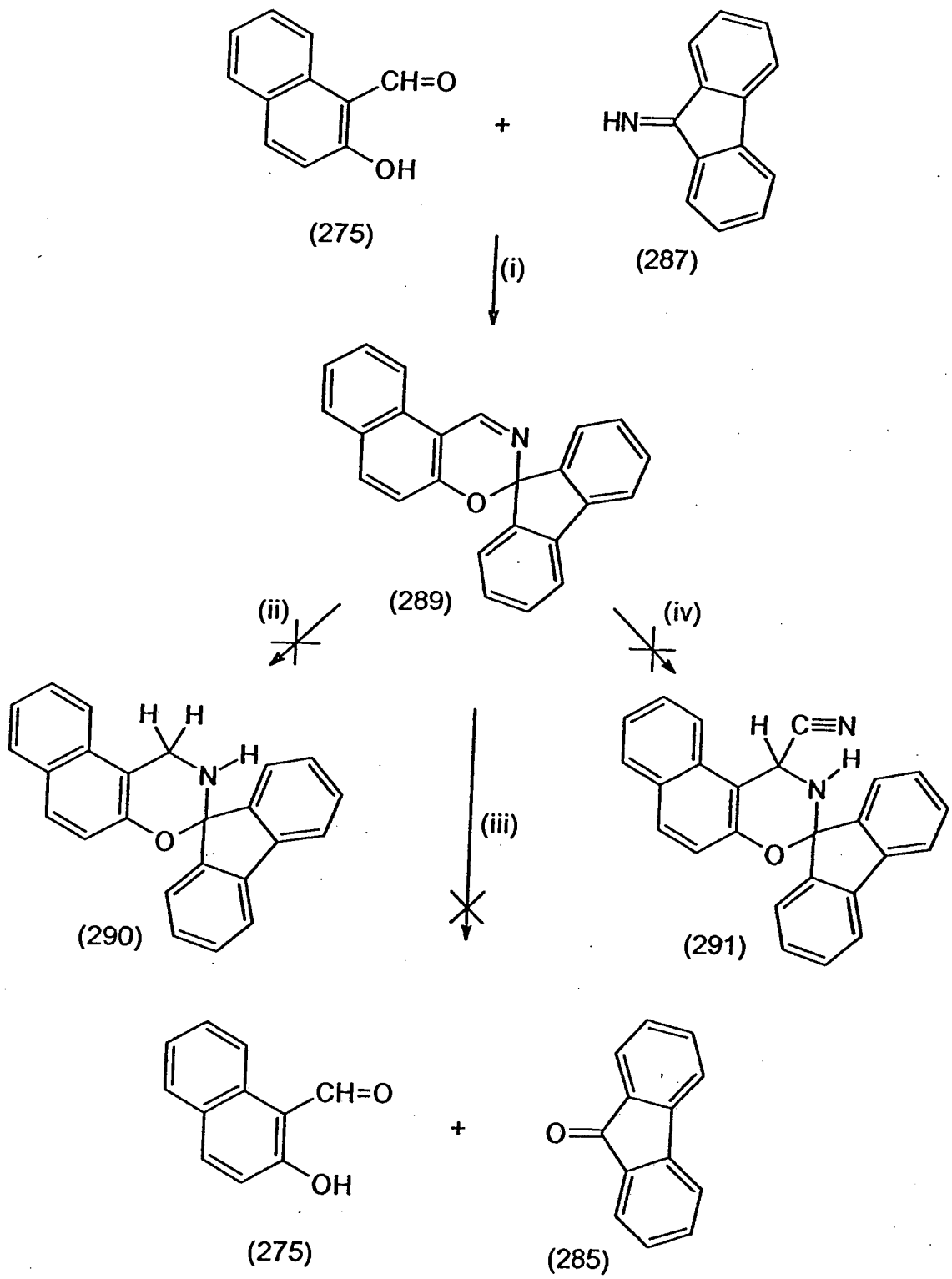
(288)

(i) $NH_3(g)$, 165°C, atmos. press.

(ii) NaN_3, MeOH, reflux.

(iii) xylene, reflux.

Scheme 69



(i) Et_3N, toluene, reflux.

(ii) H_2, Pd-C, dioxane, room temp., atmos. pressure.

(iii) HCl(aqu.), ethanol, reflux.

(iv) KCN, AcOH, room temp.

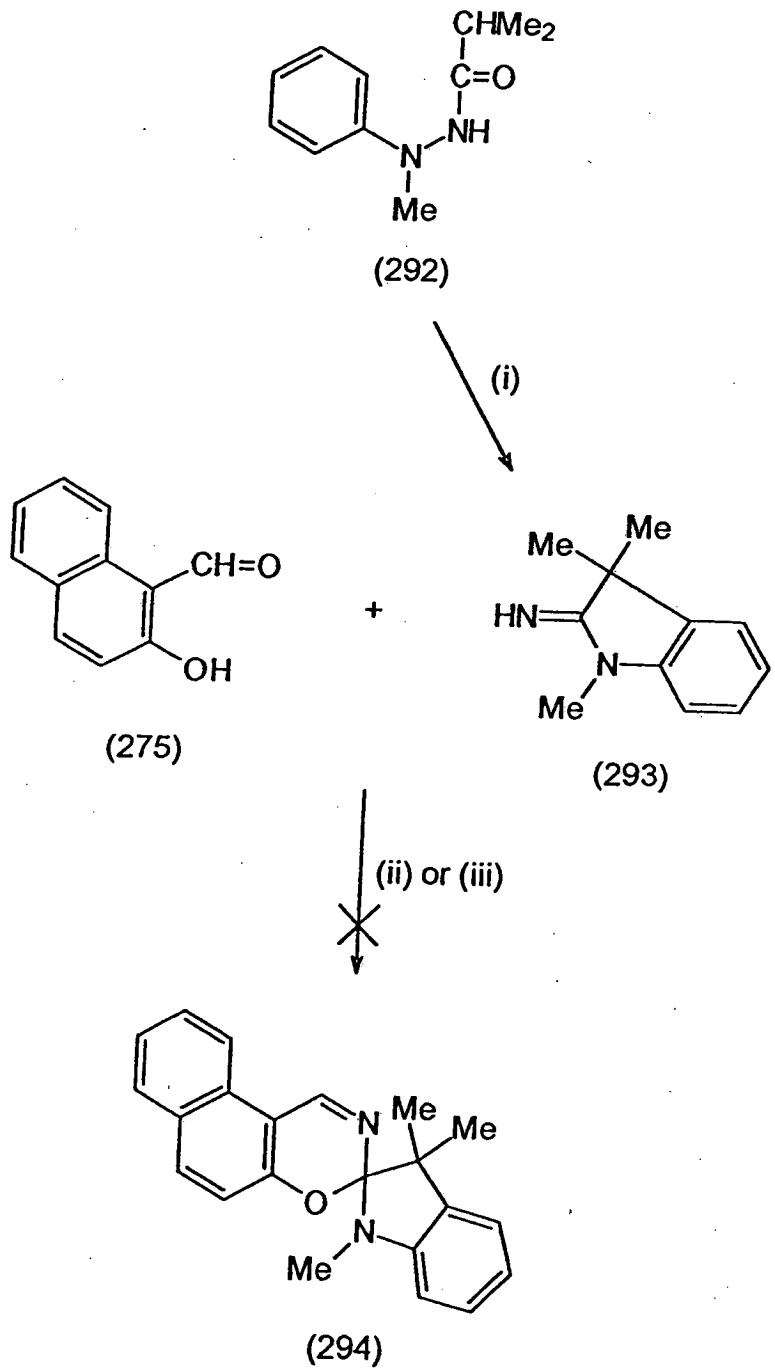
Scheme 70

aldehyde (275) was heated with the imine hydrochloride (284) and triethylamine in toluene. However, under these conditions none of the desired naphthoxazine derivative (276d) was isolated, instead an intractable gum was obtained together with unreacted auramine hydrochloride (284) (60%) and 2-hydroxy-1-naphthaldehyde (275) (38%).

Attempts were also made (Scheme 69) to prepare the known[172,173] 9*H*-fluorene-9-ketimine (287) which it was anticipated would react (Scheme 70) with 2-hydroxy-1-naphthaldehyde (275) yielding 3,3-spirofluoren-9-yl-3*H*-naphth[1,2-*e*]-1,3-oxazine (289). Initial attempts (Scheme 69) to access the fluoren-9-imine centred on a one-step synthesis[172] from fluorenone (285). Thus, fluorenone (285) was heated to 165°C and the resulting melt treated with gaseous ammonia. However, reaction under these conditions afforded none of the imine (287) giving instead a good recovery (89%) of unreacted fluorenone (285). An alternative method for the preparation of the ketimine (287) was therefore investigated. It was expected that the imine (287) could be obtained[173] by the preparation and thermolysis of the known[173] azide (288). 9-Azidofluorene (288) was prepared by reaction of 9-bromofluorene (286) with sodium azide in refluxing methanol. Under these conditions, the azide (288) was obtained in excellent yield (97%). The thermolysis of the azide (288) was effected by successive heating in toluene then xylene giving a good yield (81%) of the desired fluoren-9-imine (288).

The imine (287) was next reacted (Scheme 70) with 2-hydroxy-1-naphthaldehyde (275) in the presence of triethylamine under reflux in toluene. The product isolated from this reaction did not give a combustion analysis consistent with it being the spirofluorenylnaphthoxazine derivative (289). Several attempts were made to purify and reanalyse this product but inconsistent results were obtained. It was decided that while attempts to purify and characterise the product were ongoing, studies on preparation of derivatives should be undertaken.

The presumed naphthoxazine derivative (289) was therefore hydrogenated in the presence of palladium-on-charcoal in 1,4-dioxane at room temperature and atmospheric pressure. Under these conditions none of the desired dihydro compound (290) was isolated and the starting material was recovered unchanged in quantitative yield. The reason for the failure of this hydrogenation was thought to be that the orientation of the fluorenyl moiety, perpendicular to the oxazine ring, prevented the imino functionality from achieving close enough proximity to the catalyst for reduction to take place. An attempt was also made to react the presumed spirofluorenylnaphthoxazine derivative (289) with potassium cyanide in glacial acetic acid at room temperature. Under these conditions, none of the expected 1-cyano-1,2-dihydronaphthoxazine derivative (291) was obtained and the starting material was again recovered unchanged (77%). Heating an ethanol solution of the presumed naphthoxazine derivative (289) with aqueous hydrochloric acid



(i) $POCl_3$, toluene, 80°C then NaOH, H_2O, 50°C.

(ii) Et_3N, toluene, reflux.

(iii) ptsa, toluene then xylene, reflux (Dean and Stark).

Scheme 71

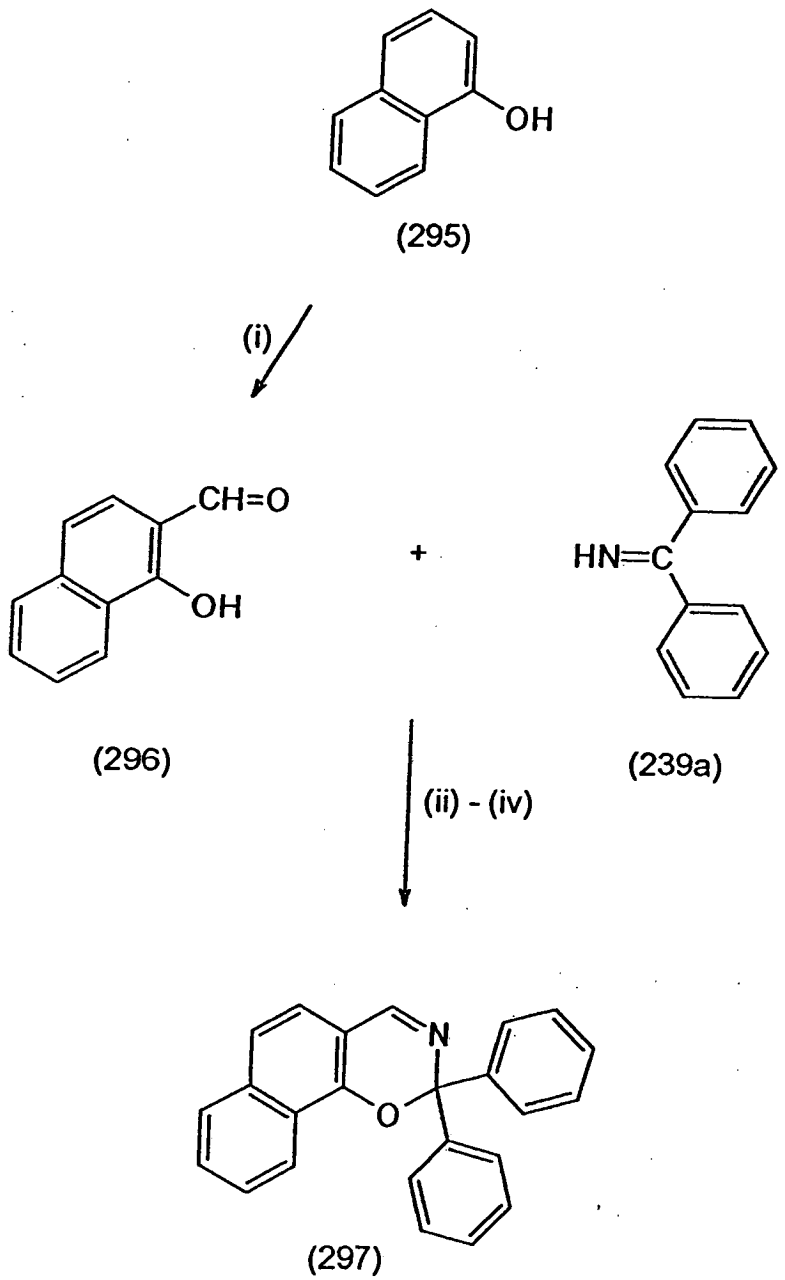
afforded no products due to hydrolysis of the oxazine ring and the starting compound was recovered in moderate yield (57%).

At this stage, a high resolution mass spectrum of the crude product of the reaction of (275) and (287) was obtained and gave a molecular ion corresponding to the naphthoxazine derivative (289) plus a further molecule of the fluoren-9-imine (287). It appears that the two species (287) and (289) are somehow complexed though the nature of this complex is unclear. Unfortunately, the mass spectrum suggesting the existence of the complex [(287):(289)] was obtained at a late stage of these studies and further investigations in this area were therefore not possible.

Work was also undertaken (Scheme 71) to prepare the previously undescribed 1,3,3-trimethylindoline-spiro[-2,3'-[3*H*]naphth[1,2-*e*]-1,3-oxazine] (294). As in previous syntheses of naphth-1,3-oxazines, work was undertaken to prepare the corresponding imine (293) whose reaction with 2-hydroxy-1-naphthaldehyde (275) was expected to give the potentially photochromic spiroindolinonaphthoxazine derivative (294). The synthesis of 3,3-dimethyl-2-imino-1-methylindoline (293), the hydrochloride salt of which is known in the literature,[174] was attempted by the preparation of the hydrazide (292) and its rearrangement in the presence of phosphorus oxychloride. Thus, 1-methyl-1-phenylhydrazine was treated with isobutyryl chloride and triethylamine in 1,2-dimethoxyethane at room temperature. Reaction under these conditions gave an excellent yield (91%) of the hydrazide (292) whose structure was supported

by its combustion analysis and its mass and ir spectra. The ^{1}H nmr spectrum of the hydrazide (292) reveals the presence of two isomers in a 1:1 ratio. The amide C-N bond would be expected to possess some double bond character and it is possible that geometric isomerism about this rotationally restricted bond is being observed. Thus, two septets due to the methine protons of the isopropyl groups are present (δ_H 2.96 and 2.41) and while in one isomer the isopropyl group gives rise to a six-proton doublet (δ_H 1.22), in the other isomer two three-proton doublets are observed (δ_H 1.18 and 1.06). The signals due to the *N*-methyl groups of both isomers are coincident (δ_H 3.16) while no signal corresponding to the N-H group of either isomer is observed. The ^{13}C nmr spectrum of the hydrazide (292) also shows more resonances than expected, further supporting the existence of *syn* and *anti* isomers. From the data available, assignment of the geometry of each isomer is not possible.

The rearrangement and cyclisation of the hydrazide (292) was effected by reaction with phosphorus oxychloride in toluene at 80°C followed work-up with aqueous sodium hydroxide. The imino-indoline (293) which was obtained from this reaction in good yield (67%) analysed correctly and gave spectroscopic data which verify its assigned structure. The ir spectrum of the imino-indoline (293) contains NH and imino absorption bands (ν_{max} 3266 and 1640 cm^{-1}) while its ^{1}H nmr spectrum contains signals due to the four aromatic protons and a three-proton singlet (δ_H 3.23) and a six-proton singlet (δ_H 1.34) due to the methyl groups. However, no signal corresponding to the imino hydrogen atom is observed.



(i) $CHCl_3$, NaOH, H_2O, EtOH, reflux.

(ii) Et_3N, toluene, reflux.

(iii) ptsa, toluene, reflux (Dean and Stark).

(iv) ptsa, 4A molecular sieves, toluene, reflux (Dean and Stark).

Scheme 72

The formation of the spiroindolinonaphthoxazine derivative (294) was next attempted by reaction of the imino-indoline (293) with 2-hydroxy-1-naphthaldehyde (275) and triethylamine in refluxing toluene. Disappointingly, none of the desired naphthoxazine derivative (294) was isolated from this reaction, instead intractable gums and a moderate recovery (56%) of the hydroxy-aldehyde (275) were obtained.

A second approach also failed to give the spiroindolinonaphthoxazine derivative (294). Reaction of the hydroxy-aldehyde (275) and the imine (293) in refluxing xylene using toluene-4-sulphonic acid as catalyst and a Dean and Stark apparatus to remove water, gave only a moderate recovery (59%) of the hydroxy-aldehyde (275). The postulated rationale for the failure (Scheme 65) of di-(4-methoxyphenyl)ketimine (239c) to react with the hydroxy-aldehyde (275) may also be used to explain this negative result. The adjacency of the indoline nitrogen to the imine functionality of (293) is likely to render the electron-rich imine unreactive toward nucleophilic attack from the hydroxyl group of the hydroxy-aldehyde (275).

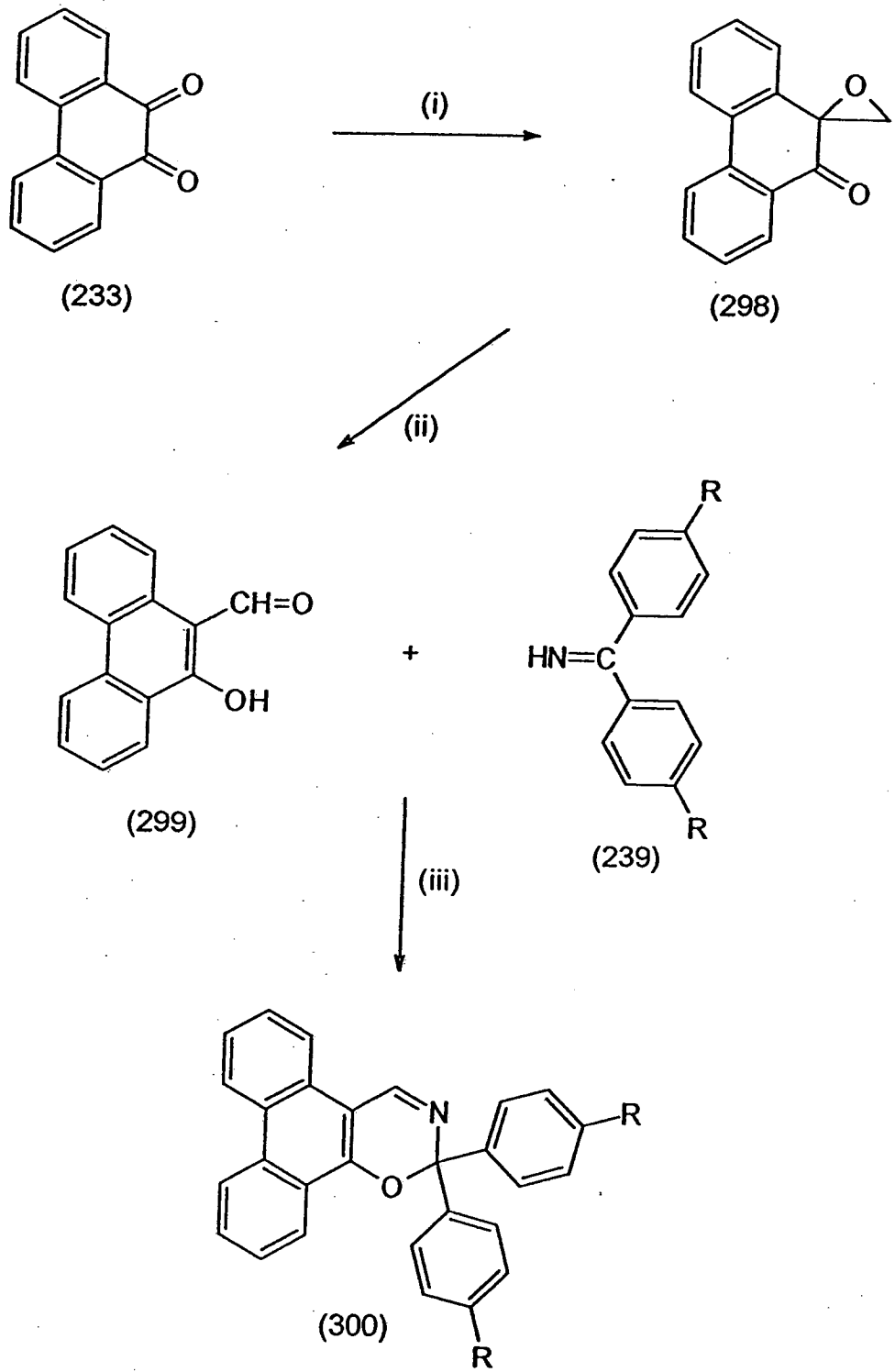
3.3 Studies on the Synthesis of 2,2-Diaryl-2*H*-naphth[2,1-*e*]-1,3-oxazine Derivatives

Studies towards these unreported but potentially photochromic structures were initially concerned with the preparation (Scheme 72) of the key starting

material, 1-hydroxy-2-naphthaldehyde (296). Unlike 2-hydroxy-1-naphthaldehyde [Scheme 71; (275)], 1-hydroxy-2-naphthaldehyde (296) is not readily commercially available and though its preparation is reported in the literature[175] it involves a very inefficient route. Owing to time pressure, a more efficient synthesis of 1-hydroxy-2-naphthaldehyde (296) was not sought and the literature[175] conditions were used. Thus, 1-naphthol (295) was reacted with chloroform and aqueous sodium hydroxide under reflux in ethanol. Under these conditions a very poor yield (2%) of the desired hydroxy-aldehyde (296) was isolated.

The reaction of the hydroxy-aldehyde (296) with diphenylketimine (239a) was next attempted. However, reaction in the presence of triethylamine under reflux in toluene gave only intractable gums. The hydroxy-aldehyde (296) was also reacted with the ketimine (239a) in refluxing toluene in the presence of toluene-4-sulphonic acid using a Dean and Stark apparatus to remove any water formed. Under these conditions a small amount (10%) of a product was isolated whose high resolution mass spectrum supports its formulation as 2,2-diphenyl-2*H*-naphth[2,1-*e*]-1,3-oxazine (297).

In an attempt to improve the efficiency of this reaction, the hydroxy-aldehyde (296) and the ketimine (239a) were heated in toluene in the presence of toluene-4-sulphonic acid and a Dean and Stark apparatus and 4Å molecular sieves employed for the removal of water. Under these conditions the diphenylnaphthoxazine derivative (297) was again isolated in very poor yield



(i) $Me_3S^+I^-$, $Bu_4N^+I^-$, NaOH, H_2O, CH_2Cl_2, 50°C.

(ii) $BF_3.Et_2O$, toluene, room temp.

(iii) Et_3N, toluene, reflux.

R
a; H
b; Me

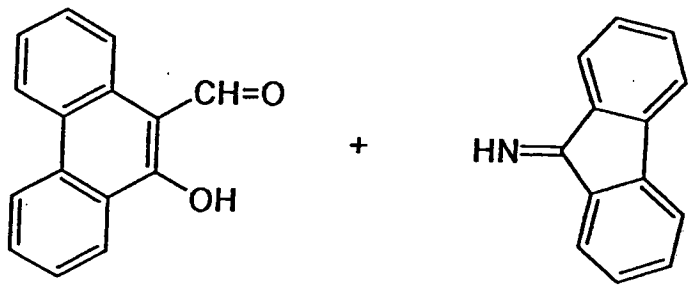
Scheme 73

(6%). Due to lack of time, no further work was possible on the synthesis of 2,2-diaryl-2*H*-naphth[2,1-*e*]-1,3-oxazines [eg (297)]. The poor yields of (279) obtained did not allow its photochromic behaviour to be studied.

3.4 Studies on the Synthesis of 2,2-Diaryl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine Derivatives

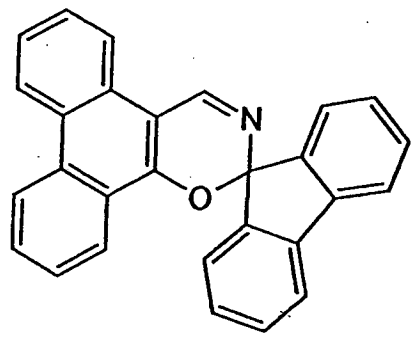
2,2-Diaryl-2*H*-phenanthro[9,10-*e*]-1,3-oxazines [Scheme 73; (300)] are unknown in the literature but are potentially useful photochromic agents. To enable the synthesis and evaluation of these new potentially photochromic compounds, preparation of the known[176,177] key starting material 10-hydroxyphenanthrene-9-carboxaldehyde (299) was required. The hydroxy-aldehyde (299) was synthesised[177] by the preparation and boron trifluoride mediated rearrangement of spiro[9*H*-10-oxophenanthrene-9-epoxide] (298). Thus 9,10-phenanthrenedione (233) was reacted with tetrabutylammonium iodide and trimethylsulphonium iodide at 50°C in dichloromethane, giving a good yield (79%) of the epoxide (298). Treatment of a toluene solution of the epoxide (298) with boron trifluoride etherate at room temperature gave a poor yield (30%) of 10-hydroxyphenanthrene-9-carboxaldehyde (299).

With the hydroxy-aldehyde (299) to hand, the synthesis of the phenanthro-oxazine derivative (300a) was attempted. Thus heating the hydroxy-aldehyde (299) with diphenylketimine (239a) and triethylamine gave a good yield (71%)



(299) (287)

(i)



(301)

(i) Et_3N, toluene, reflux.

Scheme 74

of a colourless solid product whose mass, ir and ^{1}H nmr spectra are consistent with its formulation as 2,2-diphenyl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300a). The ir spectrum shows the expected imino absorption band (ν_{max} 1646 cm^{-1}) and the ^{1}H nmr spectrum shows signals due to the aromatic protons and a one-proton singlet (δ_H 9.13) due to the imine hydrogen.

As di-(4-methylphenyl)ketimine (239b) was available, the analogous synthesis of 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300b) was also attempted. Reaction of the imine (239b) with the hydroxy-aldehyde (299) and triethylamine in refluxing toluene gave a good yield (73%) of the di-(4-methylphenyl)phenanthro-oxazine derivative (300b). The phenanthro-oxazine derivative (300b) analysed correctly and gave mass, ir and ^{1}H nmr spectra fully in accord with its assigned structure. The uv/visible spectra of the phenanthro-oxazines (300) are described at the end of this chapter (see Section 3.5, Page 278).

The preparation (Scheme 74) of 2,2-spirofluoren-9-yl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (301) was also attempted as the required starting material, the 9*H*-fluoren-9-imine (287) had been previously synthesised. The reaction of the imine (287) with 10-hydroxyphenanthrene-9-carboxaldehyde (299) was performed in refluxing toluene in the presence of triethylamine. The product of this reaction, did not give analytical and spectroscopic properties consistent with its formulation as the phenanthro-oxazine derivative (301). The analogous spirofluorenylnaphthoxazine derivative [see Page 272, Scheme 70;

(289)] was isolated as a complex with the imine (287) and it was thought likely that a similar phenomenon was being observed in this case. The high resolution mass spectrum of the product of the reaction of (299) and (287) was therefore investigated. The molecular ion which was obtained is consistent with the phenanthro-oxazine derivative (301) being present as a complex with the imine (287). The nature of this complex is unknown, and due to lack of time could not be investigated.

3.5 Ultraviolet/Visible Spectra and Photochromic Characteristics of Fused 2,2-Disubstituted 2*H*-1,3-Oxazines

Having had some success in the synthesis of fused 2*H*-1,3-oxazine derivatives, the ultraviolet/visible spectra and photochromic properties of the examples described in this chapter were investigated [see Table 11; Page 282]. The first compound to be studied was 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine [Scheme 65; (276a)]. The spectrum of a tetrahydrofuran solution of the naphthoxazine derivative (276a) was recorded then the solution was irradiated at 254 nm and its spectrum acquired once more. Comparison with the spectrum of the ring-closed form of 3,3-diphenyl-3*H*-naphth[2,1-*b*]-1,4-oxazine [see Scheme 24; (116), Pages 112-114, Table 7] reveals that prior to irradiation, the naphth-1,3-oxazine derivative (276a) gives three absorption maxima while the naphth-1,4-oxazine (116) gives only two. It should also be noted that the naphth-1,3-oxazine derivative [Scheme 65; (276a)] has a

stronger near ultraviolet absorption than the naphth-1,4-oxazine derivative [Scheme 24; (116)]. Irradiation of the tetrahydrofuran solution of 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) at 254 nm appeared to cause no photochromic response. Indeed, following irradiation, the ultraviolet/visible spectrum of the diphenylnaphthoxazine derivative (276a) was identical to that obtained before irradiation.

There are three possible conclusions which may be drawn from this absence of photochromism. The first conclusion is simply that the naphth-1,3-oxazine derivative (276a) cannot undergo the ring-opening necessary to form a coloured photoproduct. Close examination of the structure of (276a) as shown by X-ray diffraction [see Figure 6, Page 263, Tables 9 and 10] reveals that the $(Ph)_2C$-O bond [C(3)-O(4)] (fission of which would be required to effect ring opening) has a length of 1.454Å. While X-ray diffraction studies were not carried out on the diphenylnaphth-1,4-oxazine derivative [Scheme 24; (116)], X-ray data is available on the structure of 3,3-di-(4-methoxyphenyl)-3*H*-naphth[2,1-*b*]-1,4-oxazine [Scheme 39; (172)] (see Figure 4, Page 57, Tables 3 and 4). In this case the corresponding bond length [C(3)-O(4)] was calculated to be 1.4584Å. While the bond length appears to be shorter in the case of the naphth-1,3-oxazine derivative [Scheme 65; (276a)], the difference is not statistically significant and cannot be cited as a reason for the lack of photochromism exhibited by (276a).

A further possible reason why the diphenylnaphthoxazine (276a) appears to display no photochromism is that it may require activating radiation and temperature conditions other than those achievable in the laboratory. Many photochromic species also have thermochromic characteristics and it may be the case that photochromism would be observed in the diphenylnaphthoxazine (276a) at lower temperature.

The third possible conclusion which may be drawn from this lack of observed photochromism is simply that photoinduced ring-opening of the naphth-1,3-oxazine (276a) does occur but then reverses before measurements of the spectrum of the coloured form can be taken. Unfortunately, due to a lack of time, no work to verify the above hypotheses could be undertaken.

Investigation of the ultraviolet/visible spectrum of 3,3-di-(4-methylphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276b) was next undertaken. The di-(4-methylphenyl) derivative (276b) also gives three maxima in the ultraviolet region which are coincident with those due to the diphenyl compound (276a) though the extinction coefficients are lower. Following irradiation (254 nm) of a tetrahydrofuran solution of the di-(4-methylphenyl)naphthoxazine (276b) its ultraviolet/visible spectrum was found to be unchanged hence no photochromism was observed.

Similar results were obtained from the measurement of the ultraviolet/visible spectra of the 2,2-diaryl-2*H*-phenanthro[9,10-*e*]-1,3-oxazines [Scheme 73;

(300)]. 2,2-Diphenyl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300a) and 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300b) gave similar ultraviolet spectra with three maxima absorb more strongly than the corresponding naphthoxazine derivative [Scheme 65; (276a)]. No change in the spectra of the either of the phenanthro-oxazines (300) was observed on irradiation at 254 nm, hence neither of these molecules exhibit photochromism.

The foregoing chapter demonstrates the synthesis of fused 2*H*-1,3-oxazine derivatives though none of the compounds synthesised displayed photochromism. While the reason for this absence of photochromism is unclear, it remains possible that future studies may identify suitably substituted derivatives of this ring system which are photochromic.

Table 11: Ultraviolet-Visible Spectroscopic Data

Compound	Ring-closed form						After irradiation
	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm	ε_{max}	λ_{max} /nm
3,3-Diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a)	247	20705	318	6868	357	3455	no change
3,3-Di-(4-methylphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276b)	251	16795	318	6815	357	3365	no change
2,2-Diphenyl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300a)	248	35512	299	11587	359	5141	no change
2,2-Di-(4-methylphenyl)-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300b)	254	33239	299	11691	359	5235	no change

3.6 EXPERIMENTAL

General Experimental Details

For general experimental details see Chapter 2, Section 2.8, Pages 115-117.

Elemental Analyses and Mass Spectroscopic Data

Elemental analyses and mass spectroscopic data are collected in Table 12, Pages 325-326.

N-(Hydroxymethyl)phenylacetamide (253)

A suspension of phenylacetamide (54.0 g; 0.4 mol) in 4% w/v aqueous potassium carbonate solution (55.0 ml) was stirred and treated in one portion with 40% w/v aqueous formalin solution (41.3 ml; 16.5 g; 0.55 mol). The suspension was then heated briefly to 100°C until the suspended solid had dissolved then the resulting solution was allowed to cool and stirred at room temperature for 15 h.

The resulting viscous colourless suspension was filtered to give *N*-(hydroxymethyl)phenylacetamide (253) as a colourless solid (46.7 g; 71%), mp 79-81°C (lit,[166] 78°C), ν_{max} 3291 (NH), 3400-3100 br (OH) and 1659 (C=O) cm^{-1}.

1-Phenylacetamidomethyl-2-naphthol (254)

A solution of 2-naphthol (157) (25.9 g; 0.18 mol) and *N*-(hydroxymethyl)-phenylacetamide (253) (29.7 g; 0.18 mol) in ethanol (270 ml) was stirred and

treated in one portion at room temperature with concentrated hydrochloric acid (5.4 ml). The solution was then stirred and heated under reflux for 20 min then allowed to cool and stirred at room temperature for 15 h.

The resulting red-brown solution was rotary evaporated and the residue was treated with water (180 ml) and extracted several times with dichloromethane. The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give a gummy peach coloured solid (57.1 g) which was washed with ether to give 1-phenylacetamidomethyl-2-naphthol (254) as a cream solid (41.3 g; 75%), mp 136-139°C (lit,[166] 141°C), ν_{max} 3400-3000 (OH and NH) and 1622 (C=O) cm^{-1}.

1-Aminomethyl-2-naphthol Hydrochloride (255)

A solution of 1-phenylacetamidomethyl-2-naphthol (254) (40.7 g; 0.14 mol) in ethanol (700 ml) was stirred and treated in one portion at room temperature with concentrated hydrochloric acid (252 ml). The resulting colourless solution was then stirred and heated under reflux for 3 h.

The resulting pink suspension was cooled to room temperature, filtered and the solid washed with methanol to give a pink solid which was combined with a second crop obtained by rotary evaporation of the methanol mother liquor and trituration of the residual solid with ether to give the amine hydrochloride (255) (total 16.3 g; 90%) which formed pale pink microcrystals, mp 207-209°C (from ethanol-water) [lit,[166] 224-225°C (decomp)], ν_{max} 3208 (NH) cm^{-1}, δ_H [$(CD_3)_2SO$]

10.71 (1H, s, OH) (exch), 8.26 (3H, s, $^{+}NH_3$) (exch), 8.03 (1H, d, J 8.5 Hz, ArH), 7.85 (2H, d, J 8.6 Hz, ArH), 7.56-7.30 (3H, m, ArH) and 4.38 (2H, s, CH_2).

Attempted Reactions of 1-Aminomethyl-2-naphthol Hydrochloride (255) with Benzophenone (277)

(a) A solution of 1-aminomethyl-2-naphthol hydrochloride (255) (0.42 g; 0.002 mol) in 70% v/v aqueous ethanol (15.0 ml) was stirred and treated in one portion at room temperature with a solution of benzophenone (277) (0.36 g; 0.002 mol) in 70% v/v aqueous ethanol (5.0 ml). The solution was stirred and heated under reflux for 7 h then cooled and allowed to stand at room temperature for 15 h.

The resulting pink solution was rotary evaporated and the residual solid was washed with ether to give the unreacted amine hydrochloride (255) as a pale pink solid (0.30 g; 71%), mp 200°C (decomp), identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

Rotary evaporation of the ether mother liquor gave impure benzophenone (277) as an oily pink solid (0.43 g) identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with an authentic sample.

(b) A solution of benzophenone (277) (0.90 g; 0.005 mol) in anhydrous toluene (20.0 ml) was stirred and treated in one portion at room temperature

with 1-aminomethyl-2-naphthol hydrochloride (255) (1.1 g; 0.005 mol). The resulting suspension was stirred and treated at room temperature with anhydrous sodium carbonate (1.1 g; 0.01 mol) added in one portion. The suspension was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 6 h.

The suspension was cooled and allowed to stand at room temperature for 15 h then rotary evaporated under high vacuum (oil pump). The residue was treated with water (20.0 ml) and the pH was adjusted to 7-8 by the addition of concentrated hydrochloric acid then solid sodium acetate. The mixture was extracted several times with dichloromethane to give an intractable orange-brown gum (1.3 g) which yielded no identifiable material.

1-Aminomethyl-2-naphthol (259)

1-Aminomethyl-2-naphthol hydrochloride (255) (4.2 g; 0.02 mol) was treated with water (150 ml), warmed to *ca* 50°C and the resulting mixture of a flocculent purple material suspended in a pink solution was filtered to remove a small amount of intractable purple gum. The warm filtrate was treated in one portion with a solution of sodium acetate (5.0 g; 0.06 mol) in warm water (12.0 ml) and the pink solution (pH 7) was then cooled (ice bath) and stirred at 5°C for 1 h.

The resulting pale pink suspension was filtered to give impure 1-aminomethyl-2-naphthol (259) as a pale pink solid (2.9 g; 84%), mp 140-144°C (lit,[166] 115-116°C), m/z (FABMS) 174 $(M + H)^+$, ν_{max} 3200-2500 br (OH/NH_3) cm^{-1}, which could not be further purified.

The Attempted Reaction of 1-Aminomethyl-2-naphthol (259) with Formic Acid

Impure 1-aminomethyl-2-naphthol (259) (0.35 g; 0.002 mol) was treated with 98-100% formic acid (5.0 ml) and the resulting pale pink solution was stirred and heated under reflux for 3 h.

The resulting deep pink solution was rotary evaporated under high vacuum (oil pump) to give an intractable cream solid (0.26 g), from which no identifiable material could be obtained.

1-Formamidomethyl-2-naphthol (260)

Impure 1-aminomethyl-2-naphthol (259) (0.35 g; 0.002 mol) was treated with *n*-butyl formate (2.0 ml) and the suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 24 h.

The resulting yellow solution was allowed to cool then was rotary evaporated to give a gummy green-brown solid (0.27 g). This was washed with ether to give the formamide derivative (260) (0.09 g; 22%) which formed cream microcrystals, mp 165-167°C (decomp with gas evolution) [from 1,4-dioxane-

light petroleum (bp 80-100°C)], ν_{max} 3310 (NH), 3300-2800 br (OH) and 1628 (C=O) cm^{-1}, δ_H ($CDCl_3$) 9.34 (1H, s, OH) (exch), 8.17 (1H, d, J 1.7 Hz, CH=O), 7.81-7.73 (3H, m, ArH), 7.55-7.47 (1H, m, ArH), 7.38-7.20 (2H, m, ArH), 6.75-6.55 (1H, brs, NH) (part exch) and 4.83 (2H, d, J 6.7 Hz, CH_2).

1-Benzoylaminomethyl-2-benzoyloxynaphthalene (261)

(a) A solution of impure 1-aminomethyl-2-naphthol (259) (0.69 g; 0.004 mol) in anhydrous 1,4-dioxane (60.0 ml) was stirred and treated in one portion at room temperature with a solution of triethylamine (0.81 g; 0.008 mol) in anhydrous 1,4-dioxane (10.0 ml) followed by the dropwise addition of a solution of benzoyl chloride (1.1 g; 0.008 mol) in anhydrous 1,4-dioxane (10.0 ml). The resulting colourless suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The colourless suspension was filtered to remove triethylamine hydrochloride (0.89 g) and the filtrate rotary evaporated under high vacuum (oil pump). The residue was treated with water (20.0 ml) and extracted several times with dichloromethane to give a gummy cream solid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:7) gave an intractable yellow oil (0.11 g).

Elution with hexane-dichloromethane (1:4) gave the dibenzoyl derivative (261) (0.41 g; 27%) which formed colourless microcrystals, mp 218-219°C (from 1,4-dioxane), ν_{max} 3306 (NH) and 1731 and 1626 (C=O) cm^{-1}, δ_H [$(CD_3)_2SO$] 8.83 (1H, t, J 5.0 Hz, NH), 8.31-8.20 (3H, m, ArH), 8.03-7.98 (2H, m, ArH), 7.80-7.34 (11H, m, ArH) and 4.93 (2H, d, J 5.1 Hz, CH_2).

Further elution with hexane-dichloromethane (1:9) through ethyl acetate to methanol gave only a series of intractable oils and solids (total 0.49 g) from which no identifiable product was isolated.

(b) A solution of impure 1-aminomethyl-2-naphthol (259) (0.87 g; 0.005 mol) in anhydrous 1,4-dioxane (75.0 ml) was stirred and treated in one portion at room temperature with a solution of triethylamine (2.0 g; 0.02 mol) in anhydrous 1,4-dioxane (12.5 ml) followed by the dropwise addition of a solution of benzoyl chloride (2.8 g; 0.02 mol) in anhydrous 1,4-dioxane (12.5 ml). The resulting colourless suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The resulting suspension of a colourless solid in a pale yellow solution was filtered to remove triethylamine hydrochloride (1.8 g), the filtrate was rotary evaporated under high vacuum (oil pump) and the residue was treated with water (25.0 ml) then extracted several times with dichloromethane to give a gummy cream solid (2.5 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (2:3) gave an intractable amber oil (0.54 g).

Elution with hexane-dichloromethane (3:7) gave the dibenzoyl derivative (261) as a colourless solid (0.50 g; 26%), mp 212-215°C, identified by comparison (mp, ir spectrum and tlc in dichloromethane over silica) with a sample prepared in (a) before.

Further elution with hexane-dichloromethane (3:7) through ethyl acetate to methanol gave only a series of intractable gums and solids (total 0.79 g) from which no identifiable product was isolated.

1-Benzoylaminomethyl-2-naphthol (262)

(a) A suspension of the dibenzoyl derivative (261) (0.76 g; 0.002 mol) in ethanol (20.0 ml) was stirred and treated in one portion at room temperature with 1M aqueous sodium carbonate solution (2.5 ml) and the suspension was stirred and heated under reflux for 1 h.

The resulting suspension of a colourless solid in a yellow-brown solution was rotary evaporated and the residue was treated with water (5.0 ml) and filtered to give 1-benzoylaminomethyl-2-naphthol (262) (0.51 g; 92%) which formed colourless microcrystals, mp 183-185°C (from toluene), ν_{max} 3300-3050 br (OH), 3262 (NH) and 1620 (C=O) cm^{-1}, δ_H ($CDCl_3$) 10.10 (1H, s, OH) (exch),

7.91-7.72 (5H, m, ArH), 7.55-7.23 (6H, m, ArH), 7.12 (1H, d, J 0.6 Hz, NH) and 5.00 (2H, d, J 0.7 Hz, CH_2).

(b) A solution of 2-naphthol (157) (7.2 g; 0.05 mol) and *N*-(hydroxymethyl)-benzamide (263) (7.6 g; 0.05 mol) in ethanol (75.0 ml) was stirred and treated in one portion at room temperature with concentrated hydrochloric acid (1.5 ml). The orange-brown solution was stirred and heated under reflux for 20 min then cooled to room temperature and stirred for a further 17 h.

The resulting suspension of a colourless solid in a pink solution was filtered and the solid combined with a second crop obtained by rotary evaporation of the aqueous ethanol filtrate, treatment of the residue with water (50.0 ml), extraction several times with dichloromethane, washing the combined dichloromethane extracts washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporation and trituration of the residual solid with ether to give 1-benzoylaminomethyl-2-naphthol (total 11.6 g; 84%) identified by comparison [mp, ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with a sample prepared in (a) before.

<u>*N*-(Hydroxymethyl)benzamide (263)</u>

A suspension of benzamide (48.4 g; 0.4 mol) in 4% w/v aqueous potassium carbonate solution (55.0 ml) was stirred and treated in one portion at room temperature with 40% w/v aqueous formalin solution (41.3 ml; 16.5 g; 0.55 mol). The stirred mixture was heated briefly to reflux until the suspended solid

had dissolved and the resulting solution was allowed to cool, stirred at room temperature for 3 h then the resulting viscous suspension allowed to stand at room temperature for a further 16 h.

The suspension was treated with water (35.0 ml) then filtered to give *N*-(hydroxymethyl)benzamide (263) as a colourless solid (52.1 g; 86%), mp 112-115°C (lit,[167] 106-108°C), ν_{max} 3600-3200 br (OH and NH) and 1632 (C=O) cm^{-1}.

The Attempted Reaction of 1-Benzoylaminomethyl-2-naphthol (262) with Phosphorus Oxychloride in the Presence of Diisopropylethylamine

A stirred suspension of 1-benzoylaminomethyl-2-naphthol (262) (1.1 g; 0.004 mol) in anhydrous dichloromethane (15.0 ml) was treated in one portion at room temperature with diisopropylethylamine (1.6 g; 0.012 mol). The stirred mixture was cooled to 0°C (ice-salt bath) then treated dropwise with a solution of phosphorus oxychloride (0.68 g; 0.0044 mol) in anhydrous dichloromethane (5.0 ml) at such a rate that the reaction temperature was 0-5°C. The resulting suspension was stirred at room temperature with the exclusion of atmospheric moisture for 2 h.

The colourless suspension was treated dropwise with 1M aqueous sodium carbonate solution (10.0 ml) then stirred at room temperature for 1 h.

The resulting three-phase mixture was filtered to give an intractable colourless solid (0.89 g). The dichloromethane-aqueous filtrate was separated and the aqueous layer extracted several times with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give an intractable yellow-brown gum (0.45 g) from which no identifiable product could be obtained.

Diphenylketimine (239a)

Diphenylketimine (239a) was prepared by the reaction of benzonitrile (274a) with phenylmagnesium bromide (273a) as described by Pickard *et al*,[169,170] as a colourless oil (yield 63%), bp 138°C/1.5 mm Hg (lit,[170] 127°C/3.5 mm Hg), ν_{max} 3254 and 3218 (NH) cm^{-1}.

3,3-Diaryl-3*H*-naphth[1,2-e]-1,3-oxazines (276)

(a) A solution of 2-hydroxy-1-naphthaldehyde (275) (0.86 g; 0.005 mol) in anhydrous toluene (15.0 ml) was stirred and treated in one portion at room temperature with triethylamine (0.50 g; 0.005 mol) followed, dropwise by a solution of the corresponding diarylketimine (239) (0.005 mol) in anhydrous toluene (5.0 ml). The resulting brown solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for the specified time.

The brown solution was rotary evaporated under high vacuum (oil pump) to give the crude product which was purified as described for the individual reactions below.

(i) The reaction of 2-hydroxy-1-naphthaldehyde (275) with diphenylketimine (239a) for 6 h gave a gummy yellow-brown solid which was washed with ether to give 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) (72%) which formed yellow needles, mp 165-167°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1640 (C=N) cm^{-1}, δ_H ($CDCl_3$) 9.10 (1H, s, CH), 8.09 (1H, d, J 8.3 Hz, ArH), 7.87 (1H, d, J 9.6 Hz, ArH), 7.68-7.49 (6H, m, ArH) and 7.18 (8H, m, ArH).

(ii) The reaction of 2-hydroxy-1-naphthaldehyde (275) with diphenylketimine (239a) for 14 h gave a yellow brown solid which was washed with ether to give 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) as a pale yellow solid (82%), mp 161-166°C, identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

(iii) The reaction of 2-hydroxy-1-naphthaldehyde (275) with di-(4-methylphenyl)ketimine (239b) for 15 h gave a gummy brown solid which was washed with ether to give 3,3-di-(4-methylphenyl)-3*H*-naphth[1,2-*e*]-1,3-oxazine (276b) (83%) which formed cream microcrystals, mp 168-169°C (from toluene), ν_{max} 1642 (C=N) cm^{-1}, δ_H ($CDCl_3$) 9.08 (1H, s, CH), 8.08 (1H, d, J 8.3 Hz, ArH), 7.86 (1H, d, J 8.9 Hz, ArH), 7.74 (1H, d, J 7.4 Hz, ArH), 7.57-7.49 (4H, m, ArH), 7.40-7.10 (7H, m, ArH) and 2.29 (6H, s, 2 x CH_3).

(b) A stirred solution of 2-hydroxy-1-naphthaldehyde (275) (0.69 g; 0.004 mol) in anhydrous toluene (15.0 ml) was stirred and treated in one portion at room temperature with a solution of diphenylketimine (239a) (0.72 g; 0.004

mol) in anhydrous toluene (5.0 ml) followed by toluene-4-sulphonic acid monohydrate (0.076 g; 0.0004 mol). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 19 h.

The resulting suspension was hot filtered to remove some intractable solid and the solid which crystallised from the green toluene filtrate on cooling was collected and combined with a second crop obtained by washing the toluene filtrate twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 5.0 ml) then rotary evaporation and trituration of the residual gummy orange-brown solid with light petroleum (bp 40-60°C) to give 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) as a beige solid (total 0.68 g; 51%), mp 164-166°C, identified by comparison [mp, ir spectrum and tlc in hexane-ether (7:3) over silica] with a sample prepared before.

Rotary evaporation of the light petroleum mother liquor gave a red-brown oil (0.29 g) from which no further product could be obtained.

(c) 4Å Molecular sieves (1.0 g) were added to a stirred solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) and diphenylketimine (239a) (0.36 g; 0.002 mol) in anhydrous toluene (20.0 ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 40 h.

The mixture was cooled and filtered to remove the molecular sieves and the toluene filtrate was rotary evaporated to give a gummy beige solid (0.66 g) which was washed with ether to give 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) as a cream solid (0.34 g; 51%), mp 165-166°C, identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

Rotary evaporation of the ether mother liquor gave a partially crystalline brown gum (0.30 g) from which no identifiable material could be obtained.

(d) 4Å Molecular sieves (2.0 g) and toluene-4-sulphonic acid monohydrate (0.038 g; 0.0002 mol) were added at room temperature to a stirred solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) and diphenylketimine (239a) (0.36 g; 0.002 mol) in anhydrous toluene (20.0 ml). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 20 h.

The mixture was allowed to cool to room temperature and was filtered to remove the molecular sieves. The toluene filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 2.5 ml) then rotary evaporated to give a gummy brown solid (0.61 g) which was washed with ether to give 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) as a cream solid

(0.43 g; 64%), mp 154-157°C, identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with a sample prepared before.

The Acid Catalysed Hydrolysis of 3,3-Diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a)

A suspension of 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) (0.67 g; 0.002 mol) in ethanol (10.0 ml) was stirred and treated dropwise at room temperature with 2M aqueous hydrochloric acid (2.5 ml). The resulting yellow-brown solution was then stirred and heated under reflux for 1 h.

The brown solution was cooled to room temperature then was rotary evaporated and the residue was treated with water (5.0 ml) and extracted several times with dichloromethane to give a green-brown oil (0.60 g). This was triturated with ether-light petroleum (bp 40-60°C) and the insoluble material collected to give 2-hydroxy-1-naphthaldehyde (275) as a grey solid (0.11 g; 32%), mp 76-78°C (lit,[178] 82°C), identified by comparison (mp and ^{1}H nmr spectrum) with an authentic sample.

Rotary evaporation of the ether-light petroleum mother liquor gave a partially crystalline yellow-brown oil (0.41 g) which was bulb-to-bulb distilled to give benzophenone (277) as a pale yellow solid (0.36 g; 100%), bp 146°C/0.053 mm Hg, mp 40-43°C (lit,[165] 49°C), identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with an authentic sample.

1-Methyl-2-naphthol (278)

A solution of 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) (0.67 g; 0.002 mol) in anhydrous 1,4-dioxane (20.0 ml) was stirred and hydrogenated over 10% palladium-on-charcoal (0.067 g) at room temperature and atmospheric pressure for 7.5 h.

The mixture was filtered through celite and the filtrate was rotary evaporated under high vacuum (oil pump) to give an oily yellow solid (0.45 g). This was washed with light petroleum (bp 40-60°C) to give 1-methyl-2-naphthol (278) (0.27 g; 85%) which formed pale yellow microcrystals, mp 108-110°C (from light petroleum), ν_{max} 3500-3100 br (OH) cm^{-1}, δ_H ($CDCl_3$) 7.94-7.89 (1H, m, ArH), 7.79-7.74 (1H, m, ArH), 7.64-7.53 (1H, m, ArH), 7.50-7.45 (1H, m, ArH), 7.38-7.30 (1H, m, ArH), 7.06 (1H, d, J 8.8 Hz, ArH), 4.90 (1H, s, OH) (exch) and 2.54 (3H, s, CH_3).

1,2-Dihydro-3,3-diphenyl-3*H*-naphth[1,2-e]-1,3-oxazine (266)

A solution of 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) (1.3 g; 0.004 mol) in 1,2-dimethoxyethane (80.0 ml) was stirred and treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.76 g; 0.02 mol) in water (5.0 ml). The resulting orange solution was then stirred at room temperature for 72 h.

The resulting suspension was filtered to remove inorganic material, the filtrate was rotary evaporated and the residue treated with water (20.0 ml) then

extracted several times with dichloromethane to give a yellow solid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:7) gave a gummy yellow solid (0.68 g) which was washed with ether-light petroleum (bp 40-60°C) to give unreacted 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) as a yellow solid (0.51 g; 39%), mp 163-164°C, identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (3:7) over silica] with a sample prepared before.

Further elution with hexane-dichloromethane (3:7) gave a gummy green solid (0.11 g) which was washed with ether-light petroleum (bp 40-60°C) to give 1,2-dihydro-3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (266) (0.09 g; 7%) which formed yellow-green microcrystals, mp 159-166°C (from isopropanol), δ_H ($CDCl_3$) 15.35 (1H, brs, NH) (exch), 9.04 (1H, d, J 5.2 Hz, CH) (collapses to a singlet at δ_H 9.00 on D_2O shake), 7.88-7.02 (16H, m, ArH) and 5.82 (1H, d, J 2.9 Hz, CH).

1-Cyano-1,2-dihydro-3,3-diphenyl-3*H*-naphth[1,2-e]-1,3-oxazine (279)

A solution of 3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (276a) (0.67 g; 0.002 mol) in glacial acetic acid (25.0 ml) was stirred and treated with potassium cyanide (0.65 g; 0.01 mol) added in one portion at room temperature. The resulting mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 6 h.

The resulting suspension of a beige solid in an orange-brown solution was filtered and the collected solid was washed with water (10.0 ml) to give the cyanodihydronaphthoxazine derivative (279) (0.48 g; 66%) which formed colourless microcrystals, mp 143-145°C (from ethanol), ν_{max} 3356 (NH) and 1626 (NH def) cm^{-1}, δ_H ($CDCl_3$) 7.86-7.19 (16H, m, ArH), 5.42 (1H, d, J 8.5 Hz, CH) (collapses to singlet on D_2O shake) and 3.13 (1H, d, J 8.7 Hz, NH) (exch).

1-Cyano-3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (280)

Activated manganese dioxide (0.50 g) was added in one portion at room temperature to a stirred solution of 1-cyano-1,2-dihydro-3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (279) (0.36 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 20 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a gummy yellow solid (0.40 g) which was washed with ether to give 1-cyano-3,3-diphenyl-3*H*-naphth[1,2-*e*]-1,3-oxazine (280) (0.21 g; 58%) which formed cream microcrystals, mp 225-227°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1636 (C=N) cm^{-1}, δ_H ($CDCl_3$) 8.59-8.55 (1H, m, ArH), 8.06 (1H, d, J 9.0 Hz, ArH), 7.90 (1H, d, J 8.2 Hz, ArH), 7.82-7.68 (6H, m, ArH), 7.59-7.49 (2H, m, ArH) and 7.38-7.19 (5H, m, ArH).

Di-(4-methylphenyl)ketimine (239b)

Grignard quality magnesium turnings (4.8 g; 0.2 g atom) were added to a stirred solution of 4-bromotoluene (272b) (34.2 g; 0.2 mol) in anhydrous ether (120 ml) followed by one crystal of iodine. After gentle warming (oil bath) the stirred mixture refluxed spontaneously, the heat source was removed and the mixture allowed to reflux for a further 10 min. The stirred mixture was then heated under reflux for a further 15 min until dissolution of the magnesium turnings was complete.

The resulting brown solution was cooled to room temperature then treated dropwise with stirring with a solution of 4-methylbenzonitrile (274b) (21.1 g; 0.18 mol) in anhydrous ether (80.0 ml). The brown solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 15 h.

The resulting yellow suspension was cooled to room temperature and treated dropwise with methanol (40.0 g; 1.2 mol). Once the vigorous exothermic reaction had subsided, the yellow suspension was cooled to room temperature then filtered to give a yellow solid which was washed with anhydrous ether then discarded.

The combined ether filtrate and washings were rotary evaporated to give a brown oil (41.5 g) which was distilled to give a series of unidentified colourless oils (total 3.0 g), bp 48-132°C/0.075 mm Hg, followed by a pale yellow oil (25.9 g), bp 134°C/0.075 mm Hg, which crystallised on cooling to give di-(4-

methylphenyl)ketimine (239b) which formed colourless microcrystals (21.7 g; 58%), mp 68-70°C (from light petroleum) (lit,[171] 81°C), δ_H ($CDCl_3$) 9.54 (1H, s, NH) (exch), 7.48-7.44 (4H, m, ArH), 7.21 (4H, d, J 8.2 Hz, ArH) and 2.40 (6H, s, 2 x CH_3).

The Attempted Reaction of 4-Methoxybenzonitrile (274c) with 4-Methoxyphenylmagnesium Bromide (273c)

Grignard quality magnesium turnings (4.8 g; 0.2 g atom) were added to a stirred solution of 4-bromoanisole (272c) (37.4 g; 0.2 mol) in anhydrous ether (120 ml) and the stirred mixture was treated with one crystal of iodine then heated to 40°C. After 10 min an exothermic reaction began, the heat source was removed and the stirred mixture allowed to reflux for a further 10 min. The mixture was then heated under reflux for a further 15 min until dissolution of the magnesium turnings was complete. The resulting solution was cooled to room temperature and treated dropwise with stirring with a solution of 4-methoxybenzonitrile (274c) (23.9 g; 0.18 g) in anhydrous ether (80.0 ml) and the mixture heated under reflux with the exclusion of atmospheric moisture for 14 h.

The resulting yellow suspension was cooled to room temperature then was treated dropwise with methanol (40.0 g; 1.2 mol). The suspended solid became gummy then resolidified. The suspension was filtered and the collected solid discarded. The ether filtrate was rotary evaporated to give a

partially crystalline yellow oil (30.7 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) gave anisole as a colourless oil (5.0 g; 23%) identified by comparison (ir spectrum) with an authentic sample.

Elution with hexane-dichloromethane (2:3) gave unreacted 4-methoxybenzonitrile (274c) as a pale pink solid (5.5 g; 23%), mp 61-62°C (lit,[179] 57-59°C), identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (2:3) over silica] with an authentic sample.

Elution with dichloromethane gave 4,4'-dimethoxybenzophenone (132) as a cream solid (5.3 g; 14%), mp 138-140°C (lit,[160] 146°C), identified by comparison (mp and ir spectrum) with an authentic sample.

Final elution with methanol gave an intractable gummy yellow solid (6.8 g) from which no identifiable product was isolated.

Di-(4-methoxyphenyl)methyl Chloride (282)

A solution of di-(4-methoxyphenyl)methanol (281) (4.9 g; 0.02 mol) in anhydrous ether (50.0 ml) was stirred and treated with finely ground calcium chloride (4.4 g; 0.04 mol) added in one portion and the stirred suspension was cooled to 0°C (ice-salt bath) and saturated with a slow stream of anhydrous

hydrogen chloride. The resulting suspension of a colourless solid in a deep pink solution was then stoppered and stirred in the melting ice bath for 4 h.

The suspension of a colourless solid in a deep pink solution was filtered to remove inorganic material and the filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 20.0 ml), then rotary evaporated to give di-(4-methoxyphenyl)methyl chloride (282) as a pink solid (4.8 g; 91%), mp 81-83°C (lit,[148] 83-84°C).

Di-(4-Methoxyphenyl)methyl Azide (283)

A solution of di-(4-methoxyphenyl)methyl chloride (282) (2.6 g; 0.01 mol) in anhydrous dimethylformamide (25.0 ml) was stirred and treated at room temperature with sodium azide (0.65 g; 0.01 mol) added in one portion, and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 23 h.

The resulting suspension of a colourless solid in a pale yellow solution was diluted with water (50.0 ml) and extracted several times with ether and the combined ether extracts were washed with water and rotary evaporated to give the azide (283) as a cream solid (2.7 g; 100%), mp 47-50°C, ν_{max} 2092 (N_3) cm^{-1}, δ_H ($CDCl_3$) 7.29-7.20 (4H, m, ArH), 6.93 (4H, m, ArH), 5.65 (1H, s, CH) and 3.80 (6H, s, 2 x CH_3), which was used without further purification.

Di-(4-methoxyphenyl)ketimine (239c)

A solution of di-(4-methoxyphenyl)methyl azide (283) (0.54 g; 0.002 mol) in anhydrous xylene (4.0 ml) was stirred and heated under reflux with the exclusion of atmospheric moisture for 48 h.

The beige solid which separated on cooling was collected to give the imine (239c) (0.20 g; 41%) which formed cream microplates, mp 146-147°C (from hexane-ethyl acetate), ν_{max} 1621 (C=N) cm^{-1}, δ_H ($CDCl_3$) 8.40 (1H, s, NH), 7.84-7.80 (2H, m, ArH), 7.22 (2H, m, ArH), 6.98-6.90 (4H, m, ArH), 3.86 (3H, s, CH_3) and 3.82 (3H, s, CH_3).

Attempted Reactions of 2-Hydroxy-1-naphthaldehyde (275) with Di-(4-methoxyphenyl)ketimine (239c)

(a) A solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) in anhydrous toluene (6.0 ml) was stirred and treated in one portion at room temperature with triethylamine (0.20 g; 0.002 mol) followed dropwise with a solution of di-(4-methoxyphenyl)ketimine (239c) (0.48 g; 0.002 mol) in anhydrous toluene (14.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 30 h.

The resulting brown solution was allowed to cool then rotary evaporated to give a brown solid (0.82 g) which was washed with ether to afford unreacted di-(4-methoxyphenyl)ketimine (239c) as a beige solid (0.36 g; 75%), mp 132-141°C,

identified by comparison (ir spectrum and tlc in dichloromethane over silica) with a sample prepared before.

Rotary evaporation of the ether mother liquor gave impure 2-hydroxy-1-naphthaldehyde (275) as a brown solid (0.34 g; 100%), mp 67-73°C (lit,[178] 82°C), identified by comparison (ir spectrum and tlc in dichloromethane over silica) with an authentic sample.

(b) A solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) in anhydrous toluene (10.0 ml) was stirred and treated in one portion at room temperature with di-(4-methoxyphenyl)ketimine (239c) (0.48 g; 0.002 mol) in anhydrous toluene (10.0 ml) followed by toluene-4-sulphonic acid monohydrate (0.038 g; 0.0002 mol). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 24 h.

Since tlc in dichloromethane over silica showed only the presence of the starting materials, the solution was cooled and rotary evaporated under high vacuum (oil pump). The residue was treated with anhydrous xylene (20.0 ml) and the resulting yellow solution stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 63 h.

The resulting yellow-green suspension was cooled to room temperature then filtered to remove a small amount of insoluble solid and the xylene filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 2.5 ml) then rotary evaporated to give a brown gummy solid (0.69 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:1) gave unreacted 2-hydroxy-1-naphthaldehyde (275) as a gummy yellow solid (0.19 g; 56%) identified by comparison (ir spectrum and tlc in dichloromethane over silica) with an authentic sample.

Elution with hexane-dichloromethane (1:4) through dichloromethane to ethyl acetate gave only a series of intractable oils and solids (total 0.32 g) from which no identifiable material could be obtained.

The Attempted Reaction of 2-Hydroxy-1-naphthaldehyde (275) with Di-(4,4'-dimethylaminophenyl)ketimine hydrochloride (284)

A solution of 2-hydroxy-1-naphthaldehyde (275) (1.7 g; 0.01 mol) in anhydrous toluene (40.0 ml) was stirred and treated at room temperature with the imine hydrochloride (284) (3.0 g; 0.01 mol) added in one portion. The resulting suspension was treated at room temperature with triethylamine (2.0 g; 0.02 mol) added in one portion, then stirred and heated under reflux with the exclusion of atmospheric moisture for 24 h.

The resulting red-brown suspension was hot filtered to give a red-brown solid (2.1 g) which was washed with water (5.0 ml) to give unreacted imine hydrochloride (284) as an orange solid (1.8 g; 60%), mp 273°C (decomp with gas evolution) [lit,[180] 275°C (decomp with gas evolution)], identified by comparison [mp, ir spectrum and tlc in hexane-ether (2:3) over silica] with an authentic sample.

The toluene filtrate was allowed to cool then was rotary evaporated to give a brown gum (2.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (7:3) gave unreacted 2-hydroxy-1-naphthaldehyde (275) as a purple-brown solid (0.64 g; 38%), mp 83-85°C (lit,[178] 82°C), identified by comparison [mp, ir spectrum and tlc in hexane-ether (2:3) over silica] with an authentic sample.

Further elution with hexane-ether (7:3) through ether and ethyl acetate to methanol gave only a series of intractable gums and solids (total 1.6 g) from which no identifiable material could be obtained.

The Attempted Reaction of Fluorenone (285) with Ammonia

Fluorenone (285) (36.0 g; 0.2 mol) was heated to 165°C and the resulting yellow melt was stirred and treated with a slow stream of ammonia gas for 5 h.

The yellow melt was cooled to room temperature and the resulting yellow solid was dissolved in anhydrous ether (600 ml) and the solution treated with a slow stream of anhydrous hydrogen chloride until the mixture was acidic to congo red paper. The resulting suspension was filtered to remove a small amount of an intractable solid and the filtrate was rotary evaporated to give unreacted fluorenone (285) as a yellow solid (31.9 g; 89%), mp 82-86°C (lit,[181] 82-85°C), identified by comparison (mp and ir spectrum) with an authentic sample.

9-Azidofluorene (288)

A suspension of 9-bromofluorene (287) (9.8 g; 0.04 mol) in methanol (100 ml) was stirred and briefly heated to reflux and the resulting solution was cooled and treated at room temperature with sodium azide (3.9 g; 0.06 mol) added in one portion. The resulting mixture was then heated under reflux for 1.5 h.

The resulting suspension of a colourless solid in a pale yellow solution was cooled to room temperature then poured into water (300 ml) and the resulting dispersion extracted several times with ether. The combined ether extracts were washed with 2M aqueous sodium hydroxide and with water then rotary evaporated to give 9-azidofluorene (288) as a waxy pale yellow solid (8.0 g; 97%) which partially melted at 34-36°C then fully at 42-44°C (lit,[173] 43-44°C), ν_{max} 2135 and 2076 (N_3) cm^{-1}, and was used without further purification.

9*H*-Fluoren-9-imine (287)

A solution of 9-azidofluorene (288) (7.2 g; 0.035 mol) in anhydrous toluene (70.0 ml) was heated under reflux for 13 h.

The resulting pale yellow solution was allowed to cool then rotary evaporated under high vacuum (oil pump) to give a gummy yellow solid (7.0 g) shown by its ir spectrum, (ν_{max} 2135 and 2976 (N_3) cm^{-1}) to contain unreacted 9-azidofluorene (288). The crude product (7.0 g) was therefore redissolved in anhydrous xylene (70.0 ml) and the resulting pale yellow solution was stirred and heated under reflux for 5 h.

The pale yellow solution was rotary evaporated under high vacuum (oil pump) to give a gummy pale yellow solid (7.0 g) which was washed with light petroleum (bp 40-60°C) to give the 9*H*-fluoren-9-imine (287) as a pale yellow solid (5.1 g; 81%), mp 121-122°C (lit,[173] 123-124°C), ν_{max} 3190 (NH) and 1639 (C=N) cm^{-1}.

1:1 Complex of 3,3-Spirofluoren-9-yl-3*H*-naphth[1,2-*e*]-1,3-oxazine (289) and 9*H*-Fluoren-9-imine (287)

A solution of 2-hydroxy-1-naphthaldehyde (275) (3.4 g; 0.02 mol) in anhydrous toluene (60.0 ml) was treated in one portion at room temperature with triethylamine (2.0 g; 0.02 mol) then dropwise with a solution of 9*H*-fluoren-9-imine (287) (3.6 g; 0.02 mol) in anhydrous toluene (20.0 ml). The solution

was then stirred and heated under reflux with the exclusion of atmospheric moisture for 5 h.

The resulting orange-brown solution was rotary evaporated under high vacuum (oil pump) to give a gummy brown solid (7.2 g) which was washed with ether-light petroleum (bp 40-60°C) to give a 1:1 complex of 3,3-spirofluoren-9-yl-3*H*-naphth[1,2-*e*]-1,3-oxazine (289) and 9*H*-fluoren-9-imine (287) (4.2 g; 41%), mp 267°C (decomp), ν_{max} 1617 (C=N) cm^{-1}.

Rotary evaporation of the ether-light petroleum mother liquor gave a gummy brown solid (4.8 g) from which no further identifiable product could be obtained.

The Attempted Catalytic Hydrogenation of a 1:1 Complex of 3,3-Spirofluoren-9-yl-3*H*-naphth[1,2-*e*]-1,3-oxazine (289) and 9*H*-Fluoren-9-imine (287)

A solution of the naphthoxazine (289) - imine (287) complex (0.67 g; 0.0013 mol) in anhydrous 1,4-dioxane (20.0 ml) was stirred and hydrogenated over 10% palladium-on-charcoal (0.067 g) at room temperature and atmospheric pressure for 4 h.

The suspension was filtered through celite and the filtrate was rotary evaporated to give the unreacted naphthoxazine (289) - imine (287) complex as a yellow-brown solid (0.67 g; 100%), mp 262°C (decomp), identified by

comparison [mp, ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with a sample prepared before.

The Attempted Reaction of a 1:1 Complex of 3,3-Spirofluoren-9-yl-3*H*-naphth[1,2-e]-1,3-oxazine (289) and 9*H*-Fluoren-9-imine (287) with Potassium Cyanide in Acetic Acid

A solution of the naphthoxazine (289) - imine (287) complex (1.3 g; 0.0025 mol) in glacial acetic acid (50.0 ml) was stirred and treated with potassium cyanide (1.3 g; 0.02 mol) added in one portion at room temperature. The resulting mixture was then stirred at room temperature for 6 h.

The resulting red-brown solution was rotary evaporated under high vacuum (oil pump) and the residue was treated with water (20.0 ml) and extracted several times with dichloromethane. The combined dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution then rotary evaporated to give a red-brown foam which was triturated with ether-light petroleum (bp 40-60°C) to give the unreacted naphthoxazine (289) - imine (287) complex as a red-brown solid (1.0 g; 77%), mp 258°C (decomp), identified by comparison [ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with a sample prepared before.

The Attempted Acid Catalysed Hydrolysis of a 1:1 Complex of 3,3-Spirofluoren-9-yl-3*H*-naphth[1,2-e]-1,3-oxazine (289) and 9*H*-Fluoren-9-imine (287)

A suspension of the naphthoxazine (289) - imine (287) complex (0.67 g; 0.0013 mol) in ethanol (10.0 ml) was stirred and treated dropwise at room temperature with 2M aqueous hydrochloric acid (2.5 ml). The resulting brown solution was then stirred and heated under reflux for 1 h.

The brown solution was cooled then rotary evaporated to give a brown gum which was treated with water (5.0 ml) and extracted with dichloromethane (5.0 ml). The resulting three-phase mixture was filtered to give a beige solid (0.39 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:9) through ethyl acetate to methanol gave several crops of the unreacted naphthoxazine (289) - imine (287) complex as a brown solid (total 0.38 g; 57%), mp 269°C (decomp), identified by comparison [mp, ir spectrum and tlc in hexane-dichloromethane (3:7) over silica] with a sample prepared before.

2-Methylpropanoic Acid 2-Methyl-2-phenylhydrazide (292)

A solution of 1-methyl-1-phenylhydrazine (12.2 g; 0.1 mol) in anhydrous 1,2-dimethoxyethane (100 ml) was stirred and treated in one portion at room temperature with a solution of triethylamine (11.1 g; 0.11 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) followed by dropwise addition with a solution of

isobutyryl chloride (10.7 g; 0.1 mol) in 1,2-dimethoxyethane (50.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 0.5 h.

The resulting colourless suspension was filtered to remove triethylamine hydrochloride (14.1 g), and the filtrate was rotary evaporated to give a 1:1 mixture of the *syn* and *anti* isomers of the hydrazide (292) (17.4 g; 91%) which formed colourless microcrystals, mp 108-110°C (from ethyl acetate-light petroleum), ν_{max} 3187 (NH) and 1659 (C=O) cm^{-1}, δ_H ($CDCl_3$) 7.46-7.18 (4H, m, ArH) (*syn* and *anti*), 6.98-6.67 (6H, m, ArH) (*syn* and *anti*), 3.16 (6H, s, 2 x CH_3) (*syn* and *anti*), 2.96 (1H, sept, J 6.8 Hz, CH) (*syn* or *anti*), 2.41 (1H, sept, J 6.9 Hz, CH) (*anti* or *syn*), 1.22 (6H, d, J 6.9 Hz, 2 x CH_3) (*syn* or *anti*), 1.18 (3H, d, J 6.9 Hz, CH_3) (*anti* or *syn*) and 1.06 (3H, d, J 6.8 Hz, CH_3) (*anti* or *syn*), δ_C ($CDCl_3$) 182.0 (quat), 175.9 (quat), 149.5 (quat), 149.3 (quat), 129.1 (CH), 128.7 (CH), 120.4 (CH), 118.9 (CH), 113.2 (CH), 112.5 (CH), 42.6 (CH_3), 40.2 (CH_3), 32.9 (CH), 28.7 (CH), 19.1 (CH_3) and 19.0 (CH_3).

3,3-Dimethyl-2-imino-1-methylindoline (293)

A solution of the hydrazide (292) (0.96 g; 0.005 mol) in anhydrous toluene (37.5 ml) was stirred and treated with phosphorus oxychloride (2.3 g; 0.015 mol) added in one portion. The resulting solution was heated to 80°C for 24 h.

The resulting suspension of a pale blue solid in a red-brown solution was cooled to room temperature and filtered. The blue solid was dissolved in

warm water (15.0 ml) and the solution stirred and basified to pH 14 with 2M aqueous sodium hydroxide solution. The resulting emulsion was extracted several times with ether to give the imino-indoline (293) (0.58 g; 67%) which formed cream microcrystals, mp 58-60°C [from light petroleum (bp 40-60°C)], ν_{max} 3266 (NH) and 1640 (C=N) cm^{-1}, δ_H ($CDCl_3$) 7.24-7.11 (2H, m, ArH), 6.96-6.88 (1H, m, ArH), 6.73 (1H, d, J 7.8 Hz, ArH), 3.23 (3H, s, CH_3) and 1.34 (6H, s, 2 x CH_3).

Attempted Reactions of 3,3-Dimethyl-2-imino-1-methylindoline (293) with 2-Hydroxy-1-naphthaldehyde (275)

(a) A solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) in anhydrous toluene (6.0 ml) was treated at room temperature in one portion with triethylamine (0.20 g; 0.002 mol) then dropwise with a solution of 3,3-dimethyl-2-imino-1-methylindoline (293) (0.35 g; 0.002 mol) in anhydrous toluene (2.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 26 h.

The resulting orange-brown solution was rotary evaporated and the residual red-brown gum (0.85 g) was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave unreacted 2-hydroxy-1-naphthaldehyde (275) as a yellow solid (0.19 g; 56%), mp 80-83°C (lit,[178] 82°C), identified by comparison [mp, ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with an authentic sample.

Elution with hexane-ethyl acetate (4:1) through to ethyl acetate then methanol gave no further identifiable product.

(b) A solution of 2-hydroxy-1-naphthaldehyde (275) (0.34 g; 0.002 mol) in anhydrous toluene (10.0 ml) was stirred and treated in one portion at room temperature with a solution of 3,3-dimethyl-2-imino-1-methylindoline (293) (0.35 g; 0.002 mol) in anhydrous toluene (10.0 ml) followed by toluene-4-sulphonic acid monohydrate (0.038 g; 0.0002 mol). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 25 h.

Tlc in hexane-ethyl acetate (7:3) over silica showed only the presence of the starting materials and so the mixture was rotary evaporated under high vacuum (oil pump), the residue was dissolved in anhydrous xylene (20.0 ml) and the resulting brown solution stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 92 h.

The brown solution was cooled to room temperature and washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 2.5 ml) then rotary evaporated under high vacuum (oil pump) to give a red-brown gum (0.62 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave unreacted 2-hydroxy-1-naphthaldehyde (275) as a yellow-orange solid (0.20 g; 59%), mp 62-65°C (lit,[178] 82°C), identified by comparison [ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with an authentic sample.

Elution with hexane-ethyl acetate (4:1) through ethyl acetate to methanol gave no further identifiable material.

1-Hydroxy-2-naphthaldehyde (296)

1-Hydroxy-2-naphthaldehyde (296) was prepared by the reaction of 1-naphthol (295) with chloroform and sodium hydroxide as described by Hamada,[175] as a yellow-brown solid (yield 2%), mp 45-48°C (lit,[175] 53-55°C), ν_{max} 3400-3100 br (OH) and 1627 (C=O) cm^{-1}, identified by comparison (ir spectrum) with an authentic sample.

The Attempted Reaction of 1-Hydroxy-2-naphthaldehyde (296) with Diphenylketimine (239a) in the Presence of Triethylamine

A solution of 1-hydroxy-2-naphthaldehyde (296) (0.34 g; 0.002 mol) in anhydrous toluene (6.0 ml) was stirred and treated at room temperature in one portion with triethylamine (0.2 g; 0.002 mol) then dropwise with a solution of diphenylketimine (239a) (0.36 g; 0.002 mol) in anhydrous toluene (2.0 ml). The mixture was then heated under reflux with the exclusion of atmospheric moisture for 23 h.

The resulting brown solution was rotary evaporated under high vacuum (oil pump) to give a multi-component brown gum (0.67 g) which was flash-chromatographed over silica but gave no identifiable material.

2,2-Diphenyl-2*H*-naphth[2,1-*e*]-1,3-oxazine (297)

(a) A solution of 1-hydroxy-2-naphthaldehyde (296) (0.34 g; 0.002 mol) in anhydrous toluene (10.0 ml) was stirred and treated in one portion at room temperature with a solution of diphenylketimine (239a) (0.36 g; 0.002 mol) in anhydrous toluene (10.0 ml). The resulting solution was treated with toluene-4-sulphonic acid monohydrate (0.038 g; 0.0002 mol) then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 28 h.

The mixture was filtered to remove a small amount of insoluble solid and the toluene filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 2.5 ml) then rotary evaporated to give a brown gum (0.71 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:1) gave a brown oil (0.30 g) which was extracted several times with hot light petroleum (bp 40-60°C) and the combined light petroleum extracts rotary evaporated to give benzophenone (277) as a pale brown solid (0.23 g; 63%), mp 43-44°C (lit,[165] 49°C), identified by comparison [ir spectrum and tlc in hexane-dichloromethane (1:1) over silica] with an authentic sample.

Elution with hexane-dichloromethane (1:9) gave a gummy brown solid (0.14 g). This was washed with ether to give 2,2-diphenyl-2*H*-naphth[2,1-*e*]-1,3-oxazine (297) (0.07 g; 10%) which formed beige microcrystals, mp 166-168°C (from hexane-ethyl acetate).

(b) 4Å Molecular sieves (2.0 g) and toluene-4-sulphonic acid monohydrate (0.038 g; 0.002 mol) were added to a stirred solution of 1-hydroxy-2-naphthaldehyde (296) (0.34 g; 0.002 mol) and diphenylketimine (239a) (0.36 g; 0.002 mol) in anhydrous toluene (20.0 ml) at room temperature. The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 23 h.

The mixture was filtered to remove the molecular sieves and the toluene filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 2.5 ml) then rotary evaporated to give a brown oil (0.63 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave impure benzophenone (277) as a green oil (0.29 g) identified by comparison [ir spectrum and tlc in hexane-dichloromethane (2:3) over silica] with an authentic sample.

Elution with hexane-dichloromethane (2:3) gave impure 2,2-diphenyl-2*H*-naphth[2,1-*e*]-1,3-oxazine (297) as a partially crystalline brown gum (0.04 g;

6%) identified by comparison [tlc in hexane-dichloromethane (2:3) over silica] with a sample prepared before.

Spiro[9*H*-10-oxophenanthrene-9-epoxide] (298)

A suspension of 9,10-phenanthrenedione (233) (10.4 g; 0.05 mol) and tetra-butylammonium iodide (0.19 g; 0.0005 mol) in dichloromethane (150 ml) was treated in one portion at room temperature with 50% w/v aqueous sodium hydroxide solution (100 ml) followed by trimethylsulphonium iodide (10.2 g; 0.05 mol) also added in one portion. The resulting mixture was then stirred vigorously and heated at 50°C for 45 min.

The resulting green suspension was poured into water (100 ml) then extracted with ethyl acetate (50.0 ml). The resulting three-phase mixture was filtered to remove a dark green gum and the organic-aqueous filtrate was separated and the aqueous layer further extracted with ethyl acetate. Rotary evaporation of the combined organic extracts gave a yellow solid (11.2 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) through to ethyl acetate gave several crops of spiro[9*H*-10-oxophenanthrene-9-epoxide] (298) (total 8.8 g; 79%), mp 163-168°C (lit,[176,177] 164-167°C and 168-170°C), ν_{max} 1675 (C=O) cm^{-1}. Tlc in hexane-ethyl acetate (3:2) over silica revealed that the epoxide (298) was contaminated with 9,10-phenanthrenedione (233), which could not be removed by further purification.

10-Hydroxyphenanthrene-9-carboxaldehyde (299)

A solution of spiro[9*H*-10-oxophenanthrene-9-epoxide] (298) (4.4 g; 0.02 mol) in anhydrous toluene (400 ml) was stirred and treated in one portion at room temperature with a boron trifluoride etherate (6.0 ml; 0.04 mol). The resulting brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 5 min.

The resulting mixture of a brown gum in a brown solution was treated in a slow stream with 10% w/v aqueous sodium hydrogen carbonate solution (120.0 ml) then extracted with ether (40.0 ml). The resulting three-phase mixture was filtered to give an intractable red-brown solid (0.13 g) from which no identifiable product was isolated.

The organic-aqueous filtrate was separated and the aqueous layer was further extracted with ether. Rotary evaporation of the combined organic extracts gave a red-brown gum (5.3 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (9:1) gave only a series of intractable solids and oils (total 1.3 g) from which no identifiable material could be obtained.

Further elution with hexane-dichloromethane (9:1) gave a yellow solid which was crystallised from ethanol to give 10-hydroxyphenanthrene-9-carbox-

aldehyde (299) as a yellow solid (1.3 g; 30%), mp 135-137°C (lit,[176] 136-137°C), ν_{max} 1630 (C=O) cm^{-1}.

Elution with dichloromethane gave impure 9,10-phenanthrenedione (233) as a yellow solid (1.2 g), mp 181-184°C (lit,[182] 209-210°C), identified by comparison [ir spectrum and tlc in hexane-ethyl acetate (7:3) over silica] with an authentic sample.

2,2-Diaryl-2*H*-phenanthro[9,10-*e*]-1,3-oxazines

A solution of 10-hydroxyphenanthrene-9-carboxaldehyde (299) (0.22 g; 0.001 mol) in anhydrous toluene (3.0 ml) was stirred and treated at room temperature in one portion with triethylamine (0.10 g; 0.001 mol) followed by the dropwise addition of a solution of the corresponding diarylketimine (0.001 mol) in anhydrous toluene (2.0 ml). The solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 19 h.

The refluxing crude reaction mixture was worked-up as described for the individual reactions below.

(a) The reaction of the hydroxy-aldehyde (299) with diphenylketimine (239a) gave an orange-brown solution which was cooled to room temperature. The beige solid which crystallised on cooling was collected and combined with a second crop of solid obtained by rotary evaporation of the toluene mother liquor under high vacuum (oil pump) and flash-chromatography of the residual

gum over silica, eluting with hexane-ether (7:3), to give 2,2-diphenyl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300a) (total 71%) which formed colourless microcrystals, mp 219-221°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1646 (C=N) cm^{-1}, δ_H ($CDCl_3$) 9.13 (1H, s, CH), 8.65-8.55 (3H, m, ArH), 8.15-8.11 (1H, m, ArH), 7.81-7.70 (6H, m, ArH), 7.69-7.49 (2H, m, ArH) and 7.35-7.20 (6H, m, ArH).

(b) The reaction of the hydroxy-aldehyde (299) with di-(4-methylphenyl)ketimine (239b) gave an orange-brown solution which was cooled to room temperature then rotary evaporated under high vacuum (oil pump). The residual gummy orange solid was washed with ether to give 2,2-di-(4-methylphenyl)-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (300b) (73%) which formed cream microcrystals, mp 228-230°C [from toluene-light petroleum (bp 80-100°C)], ν_{max} 1645 (C=N) cm^{-1}, δ_H ($CDCl_3$) 9.11 (1H, s, CH), 8.63-8.54 (3H, m, ArH), 8.15-8.10 (1H, m, ArH), 7.81-7.48 (8H, m, ArH), 7.13-7.09 (4H, m, ArH) and 2.28 (6H, s, 2 x CH_3).

1:1 Complex of 2,2-Spirofluoren-9-yl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (301) with 9*H*-Fluoren-9-imine (287)

A solution 10-hydroxyphenanthrene-9-carboxaldehyde (299) (0.22 g; 0.001 g) in anhydrous toluene (3.0 ml) was stirred and treated at room temperature with triethylamine (0.10 g; 0.001 mol). The resulting solution was treated dropwise at room temperature with a solution fluoren-9-imine (287) (0.18 g; 0.001 mol)

in anhydrous toluene (1.0 ml) then the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 26 h.

The resulting orange suspension was hot filtered to give a 1:1 complex of 2,2-spirofluoren-9-yl-2*H*-phenanthro[9,10-*e*]-1,3-oxazine (301) with fluorene-9-imine (287) as a yellow-orange solid (0.17 g; 30%), mp 283-285°C (decomp) [from 1,4-dioxane-light petroleum (bp 80-100°C)].

Rotary evaporation of the toluene filtrate gave a gummy orange solid which was washed with ether to give a second, less pure crop of the phenanthro-oxazine (301) - imine (287) complex as an orange-brown solid (0.04 g; 7%), mp 272°C (decomp), identified by comparison [tlc in hexane-dichloromethane (3:7) over silica] with a sample prepared before.

Table12: Elemental Analysis and Mass Spectroscopic Data

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^{+a}$	C %	H %	N %	M^+, $(M+H)^{+a}$
(255) ($C_{11}H_{12}ClNO$)				174.0919 [M-Cl^-]				174.0919 [M-Cl^-]
(259) ($C_{11}H_{11}NO$)				(174)				(174)
(260) ($C_{12}H_{11}NO_2$)	71.5	5.5	6.5	201	71.6	5.5	7.0	201
(261) ($C_{25}H_{19}NO_3$)	78.5	5.3	3.7	(382)[b]	78.7	5.0	3.7	(382)
(262) ($C_{18}H_{15}NO_2$)	78.1	5.5	4.8	(278)[b]	78.0	5.4	5.1	(278)
(276a) ($C_{24}H_{17}NO$)				(336.1389)				(336.1389)
(276b) ($C_{26}H_{21}NO$)	86.4	6.0	3.5	363	86.0	5.8	3.9	363
(278) ($C_{11}H_{10}O$)	83.0	6.4	--	158	83.5	6.3	--	158
(266) ($C_{24}H_{19}NO$)	85.2	5.8	4.1	(338)	85.5	5.6	4.2	(338)
(279) ($C_{25}H_{18}N_2O$)	82.7	4.9	7.6	(363)	82.9	5.0	7.7	(363)
(280) ($C_{25}H_{16}N_2O$)	83.5	4.1	7.6	(361)	83.3	4.4	7.8	(361)

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy unless otherwise stated. [b] Molecular ion detected by Atmospheric Pressure Chemical Ionisation Mass Spectroscopy.

Table 12: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C %	H %	N %	M^+, $(M+H)^+$ [a]	C %	H %	N %	M^+, $(M+H)^+$ [a]
(239b) ($C_{15}H_{15}N$)	85.9	7.2	6.6	209	86.1	7.2	6.7	209
(283) ($C_{15}H_{15}N_3O_2$)				269.1170				269.1164
(239c) ($C_{15}H_{15}NO_2$)	74.6	6.3	5.8	(242)	74.7	6.2	5.8	(242)
(289):(287) ($C_{37}H_{24}N_2O$)				512.1889				512.1889
(292) ($C_{11}H_{16}N_2O$)	68.6	8.6	14.7	192	68.8	8.3	14.6	192
(293) ($C_{11}H_{14}N_2$)	75.7	8.1	16.0	174	75.9	8.1	16.1	174
(297) ($C_{24}H_{17}NO$)				335.1315				335.1310
(300a) ($C_{28}H_{19}NO$)	86.9	5.0	3.5	(386.1543)	87.3	4.9	3.6	(386.1545)
(300b) ($C_{30}H_{23}NO$)	86.8	5.5	3.4	(414)	87.2	5.6	3.4	(414)
(302):(287) ($C_{41}H_{26}N_2O$)				562.2038				562.2079

[a] Molecular ions / fragments detected by Electron Impact Mass Spectroscopy or, for values in parentheses, by Fast Atom Bombardment Mass Spectroscopy unless otherwise stated. [b] Molecular ion detected by Atmospheric Pressure Chemical Ionisation Mass Spectroscopy.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971.
2. 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990.
3. 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998.
4. H. Dürr, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 1.
5. R.C. Bertleson, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 10.
6. R. Guglielmetti, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 23.
7. N.Y.C. Chu, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 24.
8. G. Gauglitz, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 25.

9. K. Ichimura, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 26.

10. 'Applied Photochromic Polymer Systems', ed. C.B. McArdle, Blackie, Glasgow and London, 1992.

11. L. Chalkley, *Chem. Rev.*, 1929, **6**, 217.

12. L. Harris, J. Kaminsky and R.G. Simard, *J. Am. Chem. Soc.*, 1935, **57**, 1151.

13. C.V. Gheorghiu and V. Matei, *Bull. Soc. Chim. Fr.*, 1939, **6**, 1324.

14. C.V. Gheorghiu and B. Arruentieu, *Bull. Soc. Chim. Fr.*, 1930, **47**, 195.

15. C.V. Gheorghiu, *Bull. Soc. Chim. Fr.*, 1934, **5**, 97.

16. W. Luck and H. Sand, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 570.

17. R. Exelby and R. Grinter, *Chem. Rev.*, 1965, **65**, 247.

18. G. Priota, E. Ponsiglione and R. Ruggiero, *Tetrahedron*, 1974, **30**, 2781.

19. J. Saltiel and Y.-P. Sun, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 3.

20. D.L. Ross and J. Blanc, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 5.

21. D. Gegiou, K.A. Muzkat and E. Fischer, *J. Am. Chem. Soc.*, 1968, **90**, 3907.

22. F.B. Mallory, C.W. Mallory and S.E. Sen Loeb, *Tetrahedron Lett.*, 1985, **26**, 3773.

23. R.S. Becker and L.V. Natarajan, *Chem. Phys. Lett.*, 1986, **132**, 141.

24. W.R. Brode, E.G. Pearson and G.M. Wyman, *J. Am. Chem. Soc.*, 1954, **76**, 1034.

25. G.M. Wyman and W.R. Brode, *J. Am. Chem. Soc.*, 1951, **73**, 1487.

26. R. Pummerer and G. Marondel, *Chem. Ber.*, 1960, **93**, 2834.

27. D.L. Ross, J. Blanc and F.J. Matticoli, *J. Am. Chem. Soc.*, 1970, **92**, 5750.

28. H. Güsten, *J. Chem. Soc., Chem. Commun.*, 1969, 133.

29. C.R. Giuliano, L.D. Hess and J.D. Margerum, *J. Am. Chem. Soc.*, 1968, **90**, 587.

30. J. Weinstein and G.M. Wyman, *J. Am. Chem. Soc.*, 1956, **78**, 4007.

31. H. Rau, *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 224.

32. S. Shinkai, T. Okawa, Y. Kusano, O. Manabe, K. Kikakawa, T. Goto and T. Matasuda, *J. Am. Chem. Soc.*, 1982, **104**, 1960.

33. E. Fischer and Y. Frei, *J. Chem. Phys.*, 1957, **27**, 808.

34. E.F. Ullman and W.A. Henderson,Jr., *J. Am. Chem. Soc.*, 1966, **88**, 4942; E.F. Ullman and W.A. Henderson,Jr., *J. Am. Chem. Soc.*, 1967, **89**, 4390.

35. G.W. Griffin, K. Nishiyama and K. Ishikawa, *J. Org. Chem.*, 1977, **42**, 180.

36. A.M. Trozollo, W. Yager, G. Griffin, H. Kristinsson and I. Sarker, *J. Am. Chem. Soc.*, 1967, **89,** 3357; T. Do Minh and A.M. Trozollo, *J. Am. Chem. Soc.*, 1972, **84**, 4046.

37. R.C. Bertleson, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 3.

38. C. Schulz and H. Dürr, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 5.

39. T. Schirmeister, *Liebigs Ann. Chem.*, 1997, **9**, 1895.

40. H. Suginome, T. Mizaguchi and T. Masamune, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 987.

41. J. Daub, T. Knöchel and A. Mannscreck, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 960.

42. W.H. Laarhoven, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 7.

43. T. Wismanski-Knittel, G. Fischer and E. Fischer, *J. Chem. Soc., Perkin Trans. 2*, 1974, **15**, 1930.

44. K. Itoh, S. Tazuke and M. Sisido, *Chem. Lett.*, 1991, **2**, 257.

45. H. Hanazawa, R. Sumiya, Y. Horikawa and M. Irie, *J. Chem. Soc., Chem. Commun.*, 1992, 206.

46. S.L. Gilat, S.H. Kawai and J.-M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1993, 1439.

47. K. Uchida and M. Irie, *Chem. Lett.*, 1995, 969.

48. M. Irie, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 5.

49. E. Fischer and Y. Hirshberg, *J. Chem. Soc.*, 1952, 4522.

50. E. Fischer and Y. Hirshberg, *J. Chem. Soc.*, 1954, 297; Y. Hirshberg and E. Fischer, *J. Chem. Soc.*, 1954, 3129.

51. R. Guglielmetti, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 8.

52. A. Mustafa, *Chem. Rev.*, 1948, **43**, 509.

53. J.H. Day, *Chem. Rev.*, 1963, **63**, 65.

54. L.D. Weis, T.R. Evans and P.H. Leermaker, *J. Am. Chem. Soc.*, 1968, **90**, 6115.

55. E. Berman, R.E. Fox and F.D. Thompson, *J. Am. Chem. Soc.*, 1959, **81**, 5605.

56. P. de Mayo, A. Safardeh-Amiri and S. King-Wong, *Can. J. Chem.*, 1984, **62**, 1001.

57. K. Kimura, T. Yanashita and M. Yokoyama, *J. Chem. Soc., Perkin Trans. 2*, 1992, 613.

58. A. Samat, R. Guglielmetti and J. Meztger, *Helv. Chim. Acta.*, 1972, **55**, 1782.

59. K.H. Knauer and R. Gleiter, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 113.

60. M. Gehrtz, C. Brauchle and J. Voitländer, *J. Am. Chem. Soc.*, 1982, **104**, 2094.

61. H.G. Heller, J.R. Levell, D.E. Hibbs, D.S. Hughes and M.B. Hurshouse, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 123. (*Chem. Abstr.*, 1997, **127**, 227201)

62. K. Uchida and M. Irie, *J. Am. Chem. Soc.*, 1993, **115**, 6442.

63. K. Uchida, M. Kume and M. Irie, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 1023.

64. J.-L. Pozzo, G. Harié, V. Lokshin, A. Samat, R. Guglielmetti, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 255. (*Chem. Abstr.*, 1997, **127**, 227201)

65. I. Shimidzu, H. Kokado and E. Inoue, *Bull. Chem. Soc. Jpn.*, 1969, **42**, 1730.

66. R.C. Bertleson, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 1.

67. B. Van Gemert, A. Kumar and D.B. Knowles, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 131. (*Chem. Abstr.*, 1997, **127**, 197613)

68. B. Van Gemert, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 3.

69. N.Y.C. Chu, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 10.

70. J.C. Crano, W.S. Kwak and C.N. Welch, in 'Applied Photochromic Polymer Systems', ed. C.B. McArdle, Blackie, Glasgow and London, 1992, ch. 2.

71. Fuji Photofilm Co., Brit. Pat. 1,186,987. (*Chem. Abstr.*, 1970, **73**, 16317)

72. M. Melzig and G. Martinuzzi, PCT Int. Appl. WO 85,02,619. (*Chem. Abstr.*, 1986, **104**, 13098)

73. M. Hosoda, Eur. Pat. 141,407. (*Chem. Abstr.*, 1986, **105**, 181597)

74. W.S. Kwak and R.J. Hurditch, Eur. Pat. 141,407. (*Chem. Abstr.*, 1985, **103**, 62639)

75. C.H. Hoelscher and D.S. McBain, U.S. Pat. 4,634,767. (*Chem. Abstr.*, 1987, **106**, 176408)

76. N.Y.C. Chu, *Can. J. Chem.*, 1983, **61**, 300.

77. S. Kawanchi, H. Yoshida, N. Yomashina, M. Ohiva, S. Saeda and M. Irie, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 267.

78. S. Aramaki and G.H. Atkinson, *Chem. Phys. Lett.*, 1990, **170**, 180.

79. C. Bohne, M.G. Fan, Z.J. Li, J. Lusztyk and J.C. Scaiano, *J. Chem. Soc., Chem. Commun.*, 1990, 571.

80. F. Wilkinson, J. Hobley and M. Nofaly, *J. Chem. Soc., Faraday Trans.*, 1992, **88**, 1511.

81. G. Arnold and G. Paal, *Tetrahedron*, 1971, **27**, 1699.

82. S. Maeda, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 2.

83. H. Dürr, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 413.

84. M.H. Deniel, J. Tixier, D. Lavabre, J.C. Micheau and H. Dürr, *Mol. Cryst. Liq. Cryst.*, 1997, **298**, 129. (*Chem. Abstr.*, 1997, **127**, 221379)

85. H. Dürr, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 6.

86. J. Ito, S. Miki, R. Noda, N. Nishijima and K. Fukunishi, *Tetrahedron*, 1996, **52**, 4269.

87. H.D. Brauer and R. Schmidt, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 15.

88. S. Tokita, T. Watanabe, Y. Fujita, H. Ijima and S. Terazono, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 269. (*Chem. Abstr.*, 1997, **127**, 227202)

89. H. Bouas-Laurent and J.-P. Desvergne, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 14.

90. A. Castellan, J. Lacoste and H. Bouas-Laurent, *J. Chem. Soc., Perkin Trans. 2*, 1979, 411.

91. H. Becker, K. Sandros and K. Andersson, *Chem. Phys. Lett.*, 1981, **77**, 246.

92. J.-P. Desvergne, N. Bitit, A. Castellan and H. Bouas-Laurent, *J. Chem. Soc., Perkin Trans. 2*, 1983, 109; *J. Chem. Soc. Perkin Trans. 2*, 1988, 1885.

93. M.D. Cohen, S. Flavian and G.M.J. Schmidt, *J. Chem. Soc.*, 1964, 2041.

94. M.D. Cohen, *J. Chem. Soc. (B)*, 1968, 373.

95. E. Hadjoudis, M. Vittorakis and I. Moustakali-Mavridis, *Tetrahedron*, 1987, **43**, 1345.

96. V.A. Kumar and K. Venkateson, *J. Chem. Soc., Perkin Trans. 2*, 1991, 829.

97. J.D. Margerum and L.J. Miller, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 6.

98. A.J. Nunn and K. Schofield, *J. Chem. Soc.*, 1952, 583.

99. H.S. Mosher, C. Souers and R. Hardwick, *J. Chem. Phys.*, 1960, **32**, 1888.

100. N. Gritsan, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 167. (*Chem. Abstr.*, 1997, **127**, 212356)

101. L. Klimenko, Z. Leonenko and N. Gritsan, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 181. (*Chem. Abstr.*, 1997, **127**, 212357)

102. J. Malkin, A. Zelicheok, V. Krongauz, A.S. Dvornikov and P.M. Rentzepis, *J. Am. Chem. Soc.*, 1994, **116**, 1101.

103. V. Barachevsky, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 7.

104. A.L. Bluhm and J. Weinstein, *Nature*, 1967, **215**, 1478.

105. J.D. Margerum and L.J. Miller, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 4.

106. C.M. Bere and S. Smiles, *J. Chem. Soc.*, 1924, 2359; R. Child and S. Smiles, *J. Chem. Soc.*, 1926, 2697.

107. K.H. Knauer and R. Gleiter, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 113.

108. J. Whittall, in 'Applied Photochromic Polymer Systems', ed. C.B. McArdle, Blackie, Glasgow and London, 1992, ch. 9.

109. J. Whittall, in 'Photochromism - Molecules and Systems', Studies in organic chemistry vol. 40, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 1990, ch. 9.

110. M.G. Fan, L. Yu and W. Zhao, in 'Organic Photochromic and Thermochromic Compounds vol. 1, Main Photochromic Families', Topics in Applied Chemistry, eds. J.C. Crano and R.J. Guglielmetti, Plenum, London, 1998, ch. 4.

111. M. Tanaka, A. Miyazaki and T. Kito, Jap. Pat. 03,137634. (*Chem. Abstr.*, 1992, **116**, 72370)

112. Y. Fujimori and N. Kitamura, Jap. Pat. 05,70468. (*Chem. Abstr.*, 1993, **119**, 82994)

113. K.G. Roesner, *Mol. Cryst. Liq. Cryst.*, 1997, **298**, 243. (*Chem. Abstr.*, 1997, **127**, 163733)

114. J.J. Robillard, *Proc. SPIE - Int. Soc. Opt. Eng.*, 1997, **3227**, 296. (*Chem. Abstr.*, 1997, **127**, 235903)

115. Y. Kitmoto and T. Ochiai, Jap. Pat. 04,45997. (*Chem. Abstr.*, 1992, **117**, 181897)

116. Y. Kitmoto and T. Taniguchi, Jap. Pat. 02,164809. (*Chem. Abstr.*, 1990, **113**, 197682)

117. T. Ogiwara, Jap. Pat. 04,139109. (*Chem. Abstr.*, 1992, **117**, 118237)

118. E. Traverso, L. Crisci and N. Casilli, Eur. Pat. 315,224. (*Chem. Abstr.*, 1989, **111**, 234358)

119. Y. Kasai, M. Nakajima and E. Okanoe, Jap. Pat. 01,111007. (*Chem. Abstr.*, 1989, **111**, 19664)

120. V. Krongauz, in 'Applied Photochromic Polymer Systems', ed. C.B. McArdle, Blackie, Glasgow and London, 1992, ch. 4.

121. I. Willner, S. Rubin and T. Zor, *J. Am. Chem. Soc.*, 1991, **113**, 4013.

122. N. Nakashima, T. Nakanishi, A. Nakatani, K. Uchida and M. Irie, *Chem. Lett.*, 1996, 817.

123. N. Nakashima, T. Nakanishi, A. Nakatani, Y. Degushi, H. Murakami, T. Sagara and M. Irie, *Chem. Lett.*, 1997, 591.

124. M. Inouye, *Mol. Cryst. Liq. Cryst.*, 1997, **298**, 83. (*Chem. Abstr.*, 1997, **127**, 161638)

125. M. Takeshita and M. Irie, *Tetrahedron Lett.*, 1998, **39**, 613.

126. M. Kato and M. Irie, *J. Am. Chem. Soc.*, 1985, **107**, 1024.

127. Y. Hirshberg, *J. Am. Chem. Soc.*, 1956, **78**, 2304.

128. T. Lifka, K. Uchida and M. Irie, *Mol. Cryst. Liq. Cryst.*, 1997, **297**, 81. (*Chem. Abstr.*, 1997, **127**, 197611)

129. K. Itoh, S. Tazuke and M. Sisido, *Chem. Lett.*, 1991, 257.

130. K. Takagi, T. Kurematsu, Y. Sawaki and K. Furunawa, Jap. Pat. 02,264264. (*Chem. Abstr.*, 1990, **113**, 82310)

131. I. Cabrera, A. Dittrich and H. Ringsdorf, *Angew. Chem., Int. Ed. Engl.*, 1990, **30**, 76.

132. T. Fischer, L. Läsker, S. Czapla, J. Rübner and J. Stumpe, *Mol. Cryst. Liq. Cryst.*, 1997, **298**, 213. (*Chem. Abstr.*, 1997, **127**, 197621)

133. I. Cabrera, V. Kronkauz and H. Ringsdorf, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 1178.

134. R.J. Araujo, in 'Photochromism', Techniques of chemistry vol. 3, ed. G.H. Brown, Wiley-Interscience, New York, 1971, ch. 8.

135. U.W. Grummt, M. Reichenbacher and R. Paetzold, *Tetrahedron Lett.*, 1981, **22**, 3945.

136. M. Reichenbacher, U.W. Grummt, R. Paetzold and J. Epperlein, Ger. Pat. DD 156,372. (*Chem. Abstr.*, 1983, **98**, 135279)

137. D.M. Rowe, Ph.D. Thesis, University of Edinburgh, 1996.

138. Tokuyama Soda Company, Jap. Pat. 7,25862. (*Chem. Abstr.*, 1995, **123**, 198813)

139. Rodenstock, WO 95/00500. (*Chem. Abstr.*, 1995, **123**, 21511)

140. S. Danilov and E. Venus-Danilova, *Chem. Ber.*, 1926, **59**, 1032.

141. S. Kajigaeshe, T. Kakinami, H. Tokiyama, T. Hirakawa and T. Okamoto, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 2667.

142. T. Wieland, J. Lewalter and C. Birr, *Liebigs Ann. Chem.*, 1970, **740**, 31.

143. T.L. Ho, R.J. Hill and C.M. Wong, *Heterocycles*, 1988, **27**, 1719.

144. S.J. Cristol, J.R. Douglass and J.S. Meek, *J. Am. Chem. Soc.*, 1951, **73**, 816.

145. H.E. Zaugg and R.J. Michaels, *J. Am. Chem. Soc.*, 1958, **80**, 2770.

146. E.P. Olivetto and C. Gerold, *Org. Synth.*, Coll. vol. IV, 104.

147. R.B. Moffet, *Org. Synth.*, Coll. vol. IV, 427.

148. F. Straus and A. Dutzmann, *J. Prakt. Chem.*, 1921, **103**, 1.

149. L.A. Carpino, H.G. Chao and J.H. Tien, *J. Org. Chem.*, 1989, **54**, 4302.

150. M.P. Harcourt and R.A. More O' Ferrall, *Bull. Soc. Chim. Fr.*, 1988, 407.

151. L.F. Fieser and R.H. Brown, *J. Am. Chem. Soc.*, 1949, **71**, 3615.

152. M. Gates and W.G. Webb, *J. Am. Chem. Soc.*, 1958, **80**, 1186.

153. H. Goldschmidt, *Chem. Ber.*, 1883, **16**, 2176.

154. G. McCoy and A.R. Day, *J. Am. Chem. Soc.*, 1943, **65**, 1956.

155. J. Matheus, *Chem. Ber.*, 1888, **21**, 1886.

156. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 1, p. 5.

157. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 2, p. 1085.

158. H.E. French and K. Sears, *J. Am. Chem. Soc.*, 1858, **80**, 1186.

159. M. Tiffeneau and A. Orekehoff, *Bull. Soc. Chim. Fr.*, 1923, **33**, 1835.

160. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 2, p. 1057.

161. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 4, p. 2369.

162. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 4, p. 2504.

163. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 4, p. 2378.

164. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 5, p. 3201.

165. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 1, p. 348.

166. R.D. Haworth, R. MacGillivray and D.H. Peacock, *J. Chem. Soc.*, 1950, 1493.

167. B.P. Branchaud and P. Tsai, *J. Org. Chem.*, 1987, **52**, 5475.

168. H. Böhme and A. Ingendoh, *Annalen*, 1978, 1928.

169. P.L. Pickard and D.J. Vaughan, *J. Am. Chem. Soc.*, 1950, **72**, 876.

170. P.L. Pickard and T.L. Tolbert, *J. Org. Chem.*, 1961, **26**, 4886.

171. P.L. Pickard and D.J. Vaughan, *J. Am. Chem. Soc.*, 1950, **72**, 5017.

172. G.H. Harris, B.R. Harriman and K.W. Wheeler, *J. Am. Chem. Soc.*, 1946, **68**, 846.

173. J.P. Anselme, *Org. Prep. Proced.*, 1969, **1**, 201. (*Chem. Abstr.*, 1969, **71**, 70364)

174. A.N. Kost, G.A. Golubeva, V.G. Zabrodnyaya and Y.N. Portnov, *Khim. Geterot. Sodin. (Engl. Transl.)*, 1975, 1632.

175. C. Hamada, *J. Chem. Soc. Japan*, 1952, **73**, 47. (*Chem. Abstr.*, 1953, **47**, 9950b) (see also A. Russell and L.B. Lockhart, *Org. Synth.*, 1955, Coll. vol. III, 463)

176. B. Eistert, G. Fink and R. Wolheim, *Chem. Ber.*, 1958, **91**, 2710.

177. S.H. Alarcon, A.C. Olivieri, G.R. Labadie, R.M. Cravero and M. Gonzalez-Sierra, *Tetrahedron*, 1995, **51**, 4619.

178. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 3, p. 1747.

179. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 1, p. 248.

180. Aldrich, (cat. no., 86, 103-0)

181. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 3, p. 1441.

182. Heilbron's Dictionary of Organic Compounds (4th edn.), Eyre and Spottiswood, London, 1965, vol. 4, p. 2651.